Cervical ultrasound elastography may hold potential to predict risk of preterm birth

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ABSTRACT

INTRODUCTION: Freehand ultrasound real-time elastography (RTE) is a simple technique allowing direct visualization of the elastogramme superimposed on the B-mode image. The objective of RTE is to investigate stiffness and related parameters such as local tissue strain with a view to adding new information related to tissue morphology and architecture.

MATERIAL AND METHODS: This was a pilot study in 12 healthy pregnant women who underwent transvaginal ultrasound. The RTE (Hitachi) information was colour-coded and superimposed on the B-mode scan. Elastography images were analyzed by means of a software tool to identify thresholds for the colours red (soft), green (medium hard) and blue (hard). The cervical strain rate was measured in three different parts. Additional information obtained included age of gestation, number of pregnancies and deliveries, previous preterm births and gestational age at delivery in current pregnancy.

RESULTS: The softness of cervix increases towards portio. Within the colour spectrum, green was predominant. Strain ratio can be used as a comparative index among different subjects rather than as an absolute strain measurement.

CONCLUSION: The elastographic image allowed for easy correlation between colour distribution and the anatomical structures as it is superimposed on the B-mode image. The elasticity of the cervix increases towards portio.

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Despite numerous advances and intensive research in perinatal medicine, preterm birth and its consequences remain leading factors associated with perinatal morbidity and mortality [1]. Further, improved social conditions and obstetrical attention focused on the problem have not contributed to a reduced prevalence of preterm birth [2]. Recent years have seen an increasing interest related to screening for preterm birth with cervical elastographic measurements [3-5]. The techniques are intriguing and promising for use as non-invasive methods to study the characteristics of connective tissue.

Elastography is an imaging technique whereby local axial tissue strains are estimated from differential ultrasonic speckle displacements. These displacements are generated by a weak quasi-static stress field. The resulting strain image is called an elastogramme [6]. It is a semi-quantitative method for imaging of the elasticity of biological tissues [6]. Real-time elastography (RTE) is a technique that provides elasticity information in real time on the B-mode scans similar to colour Doppler information. In general, with ultrasound elastography, a stress is applied to the tissue and the resulting strain pattern is estimated. The strain induced in hard tissue is smaller than that observed in softer tissues. The local strain is estimated assuming that the applied stress is uniform or has a known distribution. There are two main elastographic techniques depending on whether the compression is applied automatically (transient elastography) or manually (freehand elastography) [7, 8].

The cervix is composed of smooth muscle (10%) and a large component of connective tissue (90%) consisting of collagen, elastin and macromolecular components that make up the extracellular matrix [9]. During pregnancy, collagen fibres are stabilised, for example, by decortine (PGS2) and dissolved by biglycan (PGS1) in the last trimester [10]. The physiological changes of the cervix under pregnancy are expected to affect the stiffness of the cervix and hence the strain feature. This process, called cervical ripening, results in the softening, dilatation and effacement of the cervix. The exact mechanisms controlling the cervical ripening process are largely unknown. This technique may have a role in the identification of cervical insufficiency [11]. In the present study, we wanted to test the feasibility of the RTE method.

MATERIAL AND METHODS

Study population

A total of 12 pregnant women underwent transvaginal ultrasound at an age of gestation ranging from 15 weeks and four days to 33 weeks and four days. The RTE (Hitachi) information was colour-coded and superimposed on the B-mode scan. The elastography images were analyzed by means of a software tool to identify thresholds for the colours red (soft), green (medium hard) and blue (hard). The cervix was divided into four parts The strain rate of cervix was measured in these three definite parts. The measured area is subdivided into areas A and B, of which A is the mean strain inclusion and B the mean strain reference area. The strain rate is a semi-

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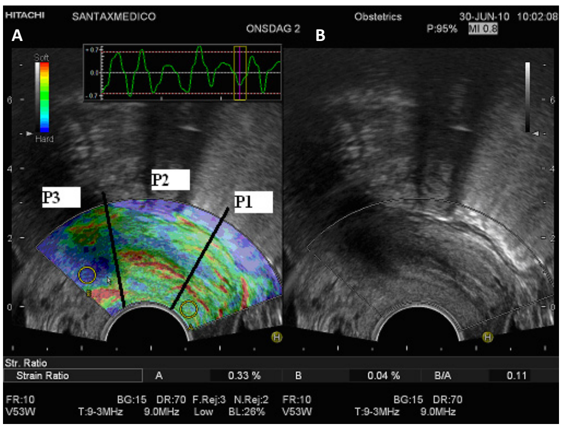
FIGURE 1

The B-mode image and the elastogramme were displayed side-by-side on the screen. Lower part P1, middle part P2, upper part P3 (about one third each) and the cervical channel. The strain rate (**A**) in P1 is higher than the strain rate (**B**) in P3, which corresponds to the colour distribution.



quantitative measurement of strain differences between two user-defined areas in an elastogramme. The middle part is the area considered more representative and reliable. An elastogramme from the B-mode scan obtained in the same sagittal plane on all cervices was stored in a standardized manner. Further, data on age of gestation, number of pregnancies and deliveries, previous preterm births, and gestational age at delivery in the current pregnancy were recorded. The pregnant women gave informed consent for participation in the examination and the study was reported to the Data Protection Agency via Region South Denmark.

Equipment

The examination of all volunteer pregnant women included B-mode scanning and RTE using the same commercially available ultrasound system (Hitachi RTE, HI VISION Preirus, Japan) and the same transducer (V53W Trans vaginal probe).

How recordings were obtained

The pregnant woman was examined lying in a gynaecological position. The cervixes were examined in longitudinal planes using B-mode ultrasound to exclude any occult abnormality. Subsequently, RTE was performed using the same machine employing the extended, combined auto-correlation method (ECAM) [12]. RTE was performed by applying light repetitive compression with the hand-held vaginal transducer over the area of interest. During the compressions, the B-mode and the elastogramme were displayed side-by-side on the screen (**Figure 1**).

Processing

The elastogramme appeared within a rectangular region of interest (ROI) as a translucent colour-coded, real-time image superimposed on the B-mode image. The strain indicator on the lateral part of the elastogramme was expressed as a numeric scale ranging from level one to six. It indicated whether the displacement was sufficient to calculate local strains within the ROI. The elastogrammes were constructed automatically using the same optimal settings throughout the study, as previously suggested by the Bergen Group [13].

Trial registration: not relevant.

RESULTS

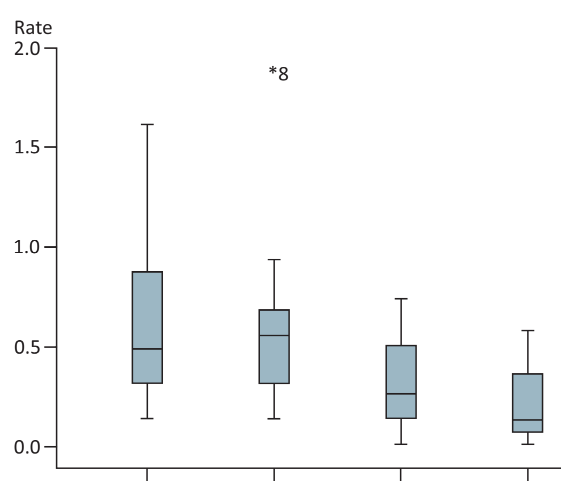
We divided the cervix into four parts: lower part P1, middle part P2, upper part P3 (about one third each) and the cervical channel (Figure 1). The cervical channel is visualized as integrated layers of green and red colours, which represent the cervical channel's histological contents. Even the glandular ditches are visualized as red depressions.

The P1 area is dominated by green and to a lesser degree red. P2 contains a range of colours, primarily blue and green layers spread almost symmetrically around the cervical channel. In P3, the layered colour distribution continues with growing dominance of the blue color.

In consequence of the colour distribution and its relation to the tissue elasticity, we conclude that P1 is more elastic (mobile) than P3, and that the elasticity of

FIGURE 2

Box plot of strain rates in the areas P1A, P2A, P2B, and P3A. Median values are marked by thick lines, interquartile ranges by boxes and minimum-maximum by bars.



P2 is a middle category between the two others. Consequently, the elasticity of the cervix increases towards the portio.

The strain rate (A) in P1 is higher than the strain rate (B) in P3, which fits with the colour distribution (Figure 1). The strain rate could be used as a comparative index among different areas rather than as an absolute strain measurement. These results can also be demonstrated using the strain levels displayed as box plots (median, interquartile range and minimum-maximum) shown in **Figure 2**, which demonstrates the above-mentioned association with the highest strains being the softest (more elastic). The median/mean strain rates (interquartile range/standard deviation) corresponding to Figure 2 are: P1A 0.49/0.61 (0.31-0.90/0.41), P2A 0.56/0.62 (0.32-0.73/0.46), P2B 0.27/0.33 (0.13-0.54/0.24) and P3B 0.14/0.21 (0.06-0.39/0.19). Stratification on previous preterm birth, deliveries, or gestational age at assessment did not change the pattern shown in Figure 2. Due to too few cases, statistical analyses are not meaningful. It is therefore not possible to draw conclusions regarding any elastographic changes in the cervix at different ages of gestation or any correlations with the length of the cervix.

DISCUSSION

Tissue elastography is a recently developed tissue characterization method for estimation of tissue stiffness. We investigated the feasibility of using ultrasound tissue elastography by evaluating uterine cervical maturation during pregnancy. The principle underlying elastography is that tissue compression produces strain (displacement) within the tissue, and that less strain occurs in hard tissue than in soft tissue. Tissue elastography thus enables the estimation of tissue stiffness by measuring compression-induced tissue strain. Elastography measures echo frequency patterns along the ultrasound beam over time before and after compression of a tissue area. At the same time, the echo frequency waves of neighbouring ultrasound waves can be compared in order to take lateral deviations around the tissue area into account.

The elastography images were analyzed by means of a software tool to identify thresholds for the colours red (soft), blue (hard) and green (medium hard). The percentages of the three colours of the total area were determined.

The results of the present study demonstrate that RTE of the cervix is a feasible method for detection of cervix elasticity and that the elastogrammes were relatively simple to produce and analyze. The elastographic image allows for easy correlation of colour distribution and anatomical structures as it is superimposed on the B-mode image.

The area close to the probe is affected more prominently than the area far from it, as the compressing pressure attenuates along the axial direction. Deeper structures are therefore displaced less than more superficial structures [8]. This applies both when scans are performed in the posterior fornix and the anterior fornix. We know that the lower part of cervix is not fixed in any way (the vaginal part) and that it moves much more than the upper part, which is attached to the uterus and ligaments and much more stable in the pelvis. It is difficult to decide if the difference of the colours is the result of the movement of the entire lower part of the cervix or rather the result of an actual change of its shape.

The area close to the probe has a better colour quality than more distant areas and a dominance of the colour green which could be a sign of qualitative colour distribution. Conversely, we observed a sharper and inhomogeneous colour distribution with dominance of the blue color that could be a sign of a less elastic or less compressed tissue.

However, as the technique is the same in all subjects, the impact of the above parameters on the appearance of the cervix is expected to be uniform. The strain ratio is the mean strain reference area (B) divided by mean strain inclusion (A). Therefore, the strain ratio can be used as a comparative index among different subjects rather than for absolute strain measurement. There is a need for a standard structure as reference area if the stain ratio is to be used as an absolute measurement. In the future, it may be possible to objectively measure the elasticity of the cervix without a reference area by using an acoustic radiation force impulse from a transvaginal tranducer [14].

This study has a number of limitations. Histological correlation of the findings was not possible as all the subjects were normal pregnant volunteers. The objective of this study was to examine the method's feasibility and to describe the elastographic patterns of the normal cervix. Further studies are therefore required to judge the effect of the above parameters and to compare the findings in women with a normal cervix to the findings in women with a short cervix.

In conclusion, RTE is a feasible and simple technique for assessing the elasticity of the cervix. The qualitative interpretation of the elastogrammes enables the discrimination of two discrete elastographic patterns of the normal pregnant cervix and may prove useful in clinical practice. Future studies are required to assess the clinical value of this method by including women in late pregnancy when the final ripening occurs associated with the transition to a soft and elastic organ and a dilatation of the cervical canal of 1-2 cm before onset of labour.

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LITERATURE

1. Goldenberg RL, Culhane JF, Iams JD et al. Epidemiology and causes of preterm birth. Lancet 2008;371:75-84.
2. Muglia LJ, Katz M. The enigma of spontaneous preterm birth. N Engl J Med 2010;362:529-35.
3. Syun-ichi Y. Tissue elastography imaging of the uterine cervix during pregnancy. J Med Ultrasonics 2007;34:209-10.
4. Thomas A, Kummel S, Gemeinhardt O et al. Real-time sonoelastography of the cervix: tissue elasticity of the normal and abnormal cervix. Acad Radiol 2007;14:193-200.
5. Swiatkowska-Freund M, Preis K. Elastography of the uterine cervix: implications for success of induction of labor. Ultrasound Obstet Gynecol 2011; 38:52-6.
6. Ophir J, Cespedes I, Ponnekanti H et al. Elastography: a quantitative method for imaging the elasticity of biological tissues. Ultrason Imag 1991;13:111-34.
7. Hall TJ, Zhu Y, Spalding CS. In vivo real-time freehand palpation imaging. Ultrasound Med Biol 2003;29:427-35.
8. Itoh A, Ueno E, Tohno E et al. Breast disease: clinical application of US elastography for diagnosis. Radiology 2006;239:341-50.
9. Danforth DN. The morphology of the human cervix. Clin Obstet Gynecol 1983;26:7-13.
10. Uldbjerg N, Ekman G, Malmstrom A et al. Ripening of the human uterine cervix related to changes in collagen, glycosaminoglycans, and collagenolytic activity. Am J Obstet Gynecol 1983;147:662-6.
11. Thomas A. Imaging of the cervix using sonoelastography. Ultrasound Obstet Gynecol 2006;28:356-7.
12. Yamakawa M, Shiina T. Strain estimation using the extended combined autocorrelation method. Japanese J App Phys (Part 1 - Regular Papers Short Notes & Review Papers) 2001;40:3872-6.
13. Havre RF, Elde E, Gilja OH et al. Freehand real-time elastography: impact of scanning parameters on image quality and in vitro intra- and interobserver validations. Ultrasound Med Biol 2008;34:1638-50.
14. Bai M, Du L, Gu J et al. Virtual touch tissue quantification using acoustic radiation force impulse technology: initial clinical experience with solid breast masses. J Ultrasound Med 2012;31:289-94.