

Prognostic value of elastography in predicting premature delivery

Zastosowanie elastografii w ocenie ryzyka wystąpienia porodu przedwczesnego

Małgorzata Świątkowska-Freund, Anetta Traczyk-Łoś, Krzysztof Preis,
Mariusz Łukaszuk, Katarzyna Zielińska

Department of Obstetrics, Medical University of Gdansk, Gdansk, Poland

Abstract

Objectives: The aim of the study was to assess changes in the consistency of the uterine cervix and correlate the obtained results with the risk of premature delivery and time from examination to delivery.

Material and methods: Elastographic images of the cervix in a group of 44 patients, admitted to the hospital due to uterine contractions before 37 weeks of gestation, were recorded and analyzed. Elastograms were assessed with the use of Elastography Index (EI), a five-step (0-4) color scale, which visualizes tissue hardness by encoding numerical values in specific colors (0 – violet/the hardest tissue; 4 – red/the softest tissue). Correlation between EI for different parts of the uterine cervix was evaluated and analyzed in relation to preterm delivery and time from examination to delivery.

Results: Twenty-one patients delivered before term and 23 at term. A strong correlation for EI of the internal os and time from examination to delivery (Pearson test, $p < 0.001$), and risk of preterm birth (Mann-Whitney-Wilcoxon test, $p < 0.001$), was noted. We also found a strong correlation between cervical canal length and risk of preterm delivery (Anova test, $p = 0.001$), and time from examination to delivery (Pearson test, $p = 0.006$).

Conclusions: Elastography may offer a chance for an objective assessment of elasticity of the uterine cervix and may become an alternative to vaginal examination and Bishop score. Proper selection of patients with high or low risk of preterm delivery may facilitate good management decisions and, consequently, decrease the percentage of immature deliveries, unnecessary medical procedures, and hospitalization.

Key words: **elastography / elastography index / preterm delivery / uterine cervix /**

Corresponding author:

M. Świątkowska-Freund
Department of Obstetrics, Medical University of Gdansk,
Kliniczna 1a, 80-402 Gdansk, Poland
tel: +48 58 349 34 45, fax: +48 58 349 34 16
e-mail: malswi@gumed.edu.pl

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Streszczenie

Cel: Celem pracy była weryfikacja możliwości oceny konsystencji szyjki macicy przy zastosowaniu elastografii oraz korelacja uzyskanych wyników z ryzykiem porodu przedwczesnego i czasem od badania do wystąpienia porodu.

Materiał i metody: Autorzy poddali analizie elastogramy szyjki macicy uzyskane podczas badania ultrasonograficznego 44 pacjentek przyjętych do szpitala z powodu czynności skurczowej mięśnia macicy przed 37 tygodniem ciąży. Obrazy elastograficzne oceniane były przy użyciu Indexu Elastograficznego (EI), gdzie pięciostopniowa skala kolorów, oddająca różnice konsystencji tkanek szyjki macicy przełożona została na skalę liczbową (0 – fiolet/najtwardsza tkanka; 4 – czerwony/najbardziej miękka tkanka). Korelacja pomiędzy EI dla poszczególnych części szyjki macicy była oceniana i analizowana w odniesieniu do ryzyka porodu przedwczesnego oraz czasu jaki upłynął od badania do wystąpienia porodu.

Wyniki: 21 pacjentek urodziło przedwcześnie, natomiast u 23 poród odbył się o czasie. Wykazano znaczącą korelację pomiędzy współczynnikiem elastograficznym ujścia wewnętrznego i wystąpieniem porodu przedwczesnego (Mann-Whitney-Wilcoxon test, $p < 0,001$), a także czasem od badania do wystąpienia porodu (Pearson test, $p < 0,001$). Autorzy stwierdzili również korelację pomiędzy długością kanału szyjki macicy a ryzykiem porodu przedwczesnego (Anova test, $p = 0,001$) i czasem od badania do porodu (Pearson test, $p = 0,006$).

Wnioski: Elastografia może pomóc w bardziej obiektywnej i wiarygodnej ocenie szyjki macicy i może stać się alternatywą dla badania wewnętrznego. Odpowiednia selekcja pacjentek do grupy wysokiego bądź niskiego ryzyka porodu przedwczesnego może pomóc we wdrożeniu właściwego postępowania, a w konsekwencji zmniejszyć liczbę porodów przedwczesnych, niepotrzebnych procedur medycznych oraz hospitalizacji.

Słowa kluczowe: **elastografia / indeks elastograficzny / poród przedwczesny / szyjka macicy /**

Introduction

Contemporary obstetrics continues to face the problem of preterm delivery, with ensuing infant mortality and morbidity as its consequences. Although the problem has been investigated by numerous researches, the rate of preterm delivery remains constant over the years, or even increased in some regions of the world [1].

It is widely accepted that changes in the consistency of the uterine cervix during pregnancy lead to labor and that preterm birth occurs if that process begins too early. Currently, the changes in the uterine cervix preceding preterm delivery are evaluated by Bishop score and ultrasonographic measurements [2, 3]. Bishop score, introduced in 1964, depends on the skills and experience of the practitioner, and is of relatively low predictive value [4]. Unfortunately, ultrasound measurements are equally unsatisfactory. Although it has been demonstrated that the likelihood of premature birth increases as the length of the cervix decreases, in many cases the infant is delivered at term, without any therapeutic intervention, despite uterine contractions and short length of the cervix in the course of pregnancy. A number of studies indicated that estimation of preterm birth likelihood is not significantly improved by the combination of Bishop score and ultrasonographic measurements with various other parameters, such as obstetrical history, clinical symptoms, and concentration of biochemical substances [5, 6, 7].

As the above mentioned methods have proven insufficient, attempts have been made to find a new tool for objective assessment of cervical consistency, including a device for measuring the vaginal portion of the cervix (CerviLenz), or software for mathematical analysis of grey-scale ultrasound image of the cervix. Unfortunately, even if these methods appear to be more reliable, complicated operating instructions adversely affect their use in clinical practice [8, 9].

So far, attempts to use elastography in the evaluation of the cervix during pregnancy have demonstrated that the new tool was

able to show the correlation between changes in the uterine cervix and reaction to oxytocin infusion at term labor [10, 11].

The objective of the study was to assess whether elastographic images of cervical consistency can be used to predict preterm delivery and what was their predictive value in comparison to Bishop score.

Methods

The study included a group of 44 pregnant women admitted to the hospital with preterm uterine contractions and intact membranes. All women were administered intravenous tocolytic agents due to persistent contractions.

Initially, all subjects were placed in the dorsal lithotomy position and examined vaginally, the cervix was assessed with Bishop score. Next, a vaginal probe was introduced to the anterior fornix of the vagina and a mid-sagittal, full-length view of the cervix was generated – measurements of the length of the cervical canal and the width of the internal os were taken. Ultrasound-derived elastography was performed simultaneously, using the same probe. After the cervix was visualized to measure the previously mentioned parameters, elastography was performed with no additional probe movements or pressure. Elastographic images of the cervix were achieved due to movement generated by patient breathing and arterial pulsation, and were operator-independent. If the probe was pressed against the cervix, or if the patient was moving or coughing, an image could not be obtained because all parts of the cervix were moving too much and visualized as ‘soft’. Informed written consent was obtained from all study participants before the elastographic examination. Elastography images were generated with a transvaginal probe using Accuvix V10 ultrasound equipment and ElastoScan software (Medison, Seoul, Korea), and a two-color number scale (violet to red). Elastograms stored on a hard drive were assessed with the use of Elastography Index (EI), five-step (0-4) color scale, which visualizes tissue hardness by encoding numerical

Table I. Correlations between EI for parts of the cervix and Bishop score, preterm delivery, and time from examination to delivery.

Part of the cervix	Correlation with cervical consistency (Pearson's test)	Correlation with Bishop score (Pearson's test)	Correlation with preterm delivery (Mann-Whitney-Wilcoxon test)	Correlation with time from examination to delivery (Pearson's test)
Anterior wall	$p=0.896$	$p=0.373$	$p=0.673$	$p=0.265$
Posterior wall	$p=0.565$	$p=0.71$	$p=0.755$	$p=0.962$
Internal os	$p=0.787$	$p=0.002$	$p<0.001$	$p<0.001$
Cervical canal	$p=0.811$	$p=0.125$	$p=0.006$	$p=0.002$
External os	$p=0.699$	$p=0.004$	$p=0.002$	$p<0.001$

values in specific colors. The hardest tissue presented in violet and was assigned 0; blue – 1; green – 2; yellow – 3; the softest area (red) was designated as 4. Elastography Index was used for the assessment of various parts of the cervix. We selected five regions of interest (ROI) in the cervix: central part of the anterior wall, central part of the posterior wall, internal and external os, middle part of the cervical canal. Then, a circle of 5mm in diameter was placed in each of the five regions (Figure 1). The best quality image was selected for the analysis, preferably containing visible amniotic fluid or urine (coded as red) and the fetal skull (coded as violet). If two or more colors were visible in the evaluated part of the cervix, then it was assigned the softest alternative. For example, if the internal os was represented by both yellow and red, it was described as having an EI of 4 - red [10]. Bishop score, including vaginal assessment of cervical consistency, was correlated with EI of all ROI, risk of preterm delivery, and time from the examination to delivery. EI of all parts of the cervix was correlated with the time of delivery (term or preterm) and time from the examination to delivery.

Digital and ultrasound examinations were performed by two independent operators. EI was calculated an independent analyst as well. Researchers were blinded to each other's results.

Normality of variables was tested using the Shapiro-Wilk test. Pearson's correlation was used to assess the relationship between EI of different parts of the cervix and Bishop score and time from examination to delivery. Correlation between EI and risk of preterm birth was evaluated using Mann-Whitney-Wilcoxon test and Anova test. The data were stored in Microsoft Excel 2010 (Microsoft Corp., Redmond, WA, USA). Statistica 7.0 (StatSoft, Cracow, Poland) was used for the statistical analysis. The level of statistical significance was determined at $p\leq 0.05$.

Results

Average patient age and gestational age at examination were 28.5 (17-43) years and 30 (22-36) weeks, respectively. As far as gravidity was concerned, 61.4% of the patients were nulliparous, while 6.8% and 2.3% of the patients had had one or two preterm labors, respectively. Deliveries took place from a few hours after the examination to even 100 days. Elastographic visualization of the cervix and calculation of EI for the particular parts was possible in all women. In the studied group, 47.7% of women delivered before term and 52.3% delivered at term. Distribution of preterm births was as follows: 34% - moderately preterm (from 33 to 36 completed weeks), 11.5% - very preterm (from 29 to 32 weeks), and 4.5% - extremely preterm (<28 weeks) birth.

Average Bishop score in the analyzed group was $3\pm SD$.

There was a statistically significant correlation between Bishop score and risk of preterm delivery (Mann-Whitney-Wilcoxon test; $p=0.002$) and the number of days from examination to delivery (Pearson test; $p=0.003$). However, we did not find any correlation between the consistency of the uterine cervix, assessed during the vaginal examination as a part of Bishop score, and the risk of preterm delivery (Mann-Whitney-Wilcoxon test; $p=0.338$).

The median EI for the anterior wall of the cervix was 0.5 points (from 0 to 4), 0.48 points (from 0 to 4) for the posterior wall, 0.9 points (from 0 to 4) for the internal os, 1.05 points (from 0 to 4) for the middle part of the canal, and 1.16 points (from 0 to 4) for the external os.

The correlations between EI for the ROI and Bishop score, preterm delivery, and time from examination to delivery are presented in Table I. The analysis of the relationship between EI of ROI and risk of preterm delivery and time from examination to delivery revealed a strong correlation for EI of the internal and external os of the cervical canal and its central part. The softer the internal orifice, i.e. the most sensitive elastographic indicator, the higher the risk of imminent delivery. Simultaneously, there was a correlation between the risk of preterm birth ($p=0.001$) or time from examination to delivery ($p=0.006$) and the length of the cervical canal. The cervical length was strongly associated with EI of the internal os ($p<0.001$). Patients with a shorter cervix had significantly softer region of the internal os as compared to patients with a longer cervix. There was no significant correlation between EI of the anterior or posterior cervical wall and preterm delivery or time from examination to labor.

The relationship between Bishop score and EI of the cervical parts demonstrated a significant correlation for EI of the external and internal os. There was no correlation between the anterior and posterior wall and the cervical canal and Bishop score. Also, no significant correlation between EI of the particular part of the cervix and its consistency was found.

Discussion

Preterm labor is defined as birth occurring before the completion of 37 weeks of gestation. In the literature, the rate of preterm delivery ranges from 5% to 25%, and constitutes the leading direct cause of perinatal mortality and morbidity worldwide. Spontaneous preterm birth remains a challenging issue due to complex pathogenesis and heterogeneity of risk factors. Although understanding of the underlying mechanisms of the cervical ripening facilitates treatment planning, it does not help to establish the most important element, i.e. timely diagnosis [11].

During the last few decades, changes in the uterine cervix preceding delivery were evaluated only by subjective methods. Bishop score, which describes the result of vaginal examination, has little prognostic value in terms of preterm delivery risk. Our study showed a correlation between Bishop score and time from examination to spontaneous delivery and preterm delivery, but it did not demonstrate any correlation with cervical consistency. That finding confirms the subjectivity of vaginal examination, especially while evaluating tissue softness. Elastography may offer a possibility of objective assessment of elasticity of the uterine cervix and may become an alternative to subjective vaginal examination [12, 13]. The possibility of assessing parts of the cervix that are not available during a vaginal examination, namely the internal os and the superior parts of the cervical canal, constitutes an additional benefit of the exam. In contrast, during a standard vaginal examination, only the vaginal portion of the cervix and the external os, their consistency and dilatation, can be assessed.

Correlation between EI of tissue around the internal and the external os, or the central part of the cervical canal and risk of preterm birth or time from examination to delivery is the main finding of our study. We demonstrated that EI of the internal os seems to be the most sensitive elastographic indicator, additionally associated with the cervical length, suggesting that elastography might constitute a complementary method, together with cervical canal ultrasound measurement, in establishing preterm delivery prognosis. Hernandez-Andrade et al., performed cervical elastography in 262 patients between 8-40 weeks of gestations and reported reduction in cervical stiffness with decreasing cervical length and advancing gestational age, mainly manifested in the internal os [14]. The work of Fuchs et al., revealed a statistically significant correlation between the cervical length and the elasticity of the anterior cervical labium, what confirms that the changes in the cervical texture occur simultaneously with the changes of the cervical length [15].

Increasing value of EI of the internal os of the cervical canal, which corresponds to softer consistency, may constitute a more sensitive predictor of approaching preterm labor, aiding in differentiating between patients eligible for hospitalization and/or pharmacotherapy. Consequently, appropriate selection of patients with and without the actual risk of premature delivery may decrease the percentage of unnecessary procedures and hospitalization.

Ways of improving detection of women with risk of premature delivery still remain an open matter. The rate of spontaneous preterm births has been known to be positively associated with maternal levels of several biomarkers, but systematic review of the literature on premature birth biomarkers (116 biomarkers investigated in the last 40 years) revealed these factors to be either nonspecific or detected too late [16, 17, 18].

To date, only the presence of fetal fibronectin in vaginal secretions of symptomatic patients reliably defines the subgroup at increased risk for preterm delivery [18]. The same changes which are responsible for positive fibronectin test cause visualization of the internal orifice in elastograms and higher values of EI for the mentioned parts of the cervix. Plausibly, the joint employment of these two methods may improve prediction rates of preterm delivery.

Conclusions

Elastography seems to be a promising tool for objective evaluation of the changes in the consistency of the uterine cervix during pregnancy. Also, there is a correlation between the elasticity of the internal os and the cervical length, suggesting that elastography might constitute a complementary method, together with cervical canal ultrasound measurement, in establishing the diagnosis of preterm delivery. Further studies of elastography and its correlation with other methods of predicting preterm delivery are needed in order to assess the clinical value of the method.

Oświadczenie autorów

1. Małgorzata Świątkowska-Freund – autor koncepcji pracy, założeń metod, analizy oraz interpretacji danych, napisanie pracy, analiza statystyczna - autor zgłaszający i odpowiedzialny za manuskrypt.
2. Anetta Traczyk-Łoś – wykonanie badań, gromadzenie danych, analiza i interpretacja danych, napisanie pracy, tłumaczenie pracy na j. angielski.
3. Krzysztof Preis – autor koncepcji, założeń oraz metod pracy, analiza oraz interpretacja danych.
4. Mariusz Łukaszuk – wykonanie badań tłumaczenie pracy na j. angielski.
5. Katarzyna Zielińska – analiza statystyczna, wykonanie badań.

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