Clinical applications of uterine cervical length assessment by transvaginal ultrasonography for preventing preterm birth

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Abstract

Cervical length measured by transvaginal ultrasound is an effective screening test for preterm birth risk assessment. It has a good diagnostic value on all studied population groups. In symptomatic patients, the measurement of the cervical length by ultrasonography allows reducing the number of hospitalizations and focusing on the cases that really need a treatment. This method could be associated with existing routine mid-trimester ultrasound scan. Performed at 19-24 weeks, cervical length screening selects asymptomatic women with increased risk of preterm birth who could benefit from effective prophylaxis. Recent evidence supports administration of vaginal progesterone to asymptomatic low risk women with short cervix (less than 20 mm). Cervical cerclage or tracheloplasty can be reserved for a minority who develop a short cervical length by progesterone treatment resistance (less than 15 mm) or has a history of spontaneous preterm birth (less than 25 mm). In this regards, cervical length screening should become a routine to all pregnant women.
Keywords: *cervical cerclage, cervical length, preterm birth, progesterone, ultrasonography*

Abbreviated words: *PTB= preterm birth; CL= cervical length; IO= internal os*

1. Introduction

Preterm birth (PTB) is the main cause of neonatal mortality and morbidity, representing 60-80% of the neonatal deaths without congenital anomalies. It has considerable implications for the medical insurance systems, education and social security. The current incidence varies between 5-9% from the total births in Europe and other developed countries[1]. The spontaneous premature birth, with or without the premature rupture of membranes, represents two thirds of the PTB, the rest resulting from obstetrical situations such as preeclampsia, intra-uterine growth restriction or multiple pregnancies[2].

Normally, the risk of PTB is assessed using clinical factors such as: multiple pregnancy, PTB antecedents or cervical surgery, and ethnicity. However, more than a half of all the premature births occur in women without clinical risk factors[3]. The assessment of predictive factors suggests that the cervical length (CL) measured by transvaginal ultrasonography is the best prediction factor of PTB, especially in the pregnancies with increased risk[4]. The uterine ultrasound receives more and more support amongst the obstetricians. Replying on this data, recent randomized clinical studies have assessed the efficacy of different clinical methods, such as progesterone and cervical cerclage or tracheloplasty, also known as a cervical stitch, in the PTB prevention. This review presents the ultrasonographic technique of cervical measurement and the current clinical strategies in case of singleton pregnancies diagnosed with shortening cervix in the mid-trimester. The study is focused on progesterone and cervical cerclage effects in two subgroups of asymptomatic pregnant women, at low risk and with a history of spontaneous PTB.

2. The CL measurement technique

The CL is currently measured by transvaginal ultrasonography, being the most precise, reproducible and predictable method. The technique was completely described[5] and is presented in Table 1[6].

In comparison with the digital examination, the ultrasound determination of the CL is less subjective, has a more reduced inter-observer variation and allows the examination of the entire cervical length, since the supravaginal portion and the internal os (IO) of the cervical canal is not accessible to the clinical examination[7].

Transvaginal measurement of the CL also has better results compared to the abdominal or transperineal scan. Thus, a correct image is difficult to achieve transabdominally and the measurements are imprecise, the distance between the probe and the cervix being large[8]. Moreover, the necessity of emptying the bladder in order to avoid the artificial lengthening of the cervix reduces the successful chances of a transabdominal scan[9]. Transabdominal measurement of the cervix is imprecise and must not be used for the prediction of preterm births[6]. Transperineal ultrasonography, although feasible in the majority of cases[10], is variable and is less correlated with the transvaginal ultrasound, the main problem being the difficult appreciation of the IO[11].

Table 1	Technique of measuring the cervical length by transvaginal ultrasonography (after Berghella and colleagues)[6]
Empty bladder, patient in supine position	
Vaginal probe of 5-7 MHz, covered by condom	
Ultrasound probe guided into anterior fornix	
A sagittal image of the cervix is obtained, with echogenic endocervical mucosa visible along the entire length of the canal	
Withdraw probe until blurred, then reinsert, avoiding an excessive pressure	
Enlarge the image (at least 2/3 of the screen)	
Obtain symmetric image of the entire endocervical canal, with internal os at flat or isosceles angles, and symmetric view of external os (anterior lip diameter must be equal to posterior lip diameter)	
Measure the entire length of the cervical canal, from internal to external os. If endocervical line is extremely concave, measure from several straight lines that approximate its general shape	
Obtain three measurements, use shortest best	
Apply fundal pressure for at least 15 seconds	
Average examination duration: 5 minutes	

The measurement of the CL must be achieved by personnel with adequate training, with a continuous evaluation of the determinations' quality. Achieved in this manner, the method has a high reproducibility, with an inter- and intra-observer variability less than 10%[7]. This precision is obtained only after about 50 supervised scans[6].

The "static" assessment of the CL can be completed by a "dynamic" one. This consists in applying a moderate fundic pressure for emphasizing a cervical modification that translates into incompetence[12,13]. Nevertheless, there is no evidence that this technique improves the prediction capacity of the preterm birth[11].

Thus, after an examination of about 5 minutes, with three measurements achieved before and after applying a fundic pressure, the shortest and best measurement (in millimeters) is reported for clinical use.

3. Clinical applications

It is know that the smaller CL, the higher will be the PTB risk. Still, the capacity of the CL to predict PTB depends on the studied population, the gestational age at which the determination is made and the limit considered for defining the preterm birth. The best studies currently use the screening of CL at 16-24 weeks and evaluate the frequency of PTB before 35 weeks of gestation. Generally, three categories of populations were studied:

■ Symptomatic pregnant women, who present with clinical symptomatology associated with uterine contractions and modifications of the cervix. These correspond to the diagnosis of threatening of premature labor ("menace d'accouchement premature").

■ Asymptomatic pregnant women, but considered with high risk for PTB: with prior PTB, uterine anomalies, cervical surgery, repeated abortions over 13 gestational weeks. Multiple pregnancies are generally included in this group.

■ Pregnant women from the general population with low risk for PTB (defined as nulliparous and women with no history of PTB).

4. Clinical applications in symptomatic pregnant women

In this group, the predictive capacity of the CL was mainly assessed in the hospitalized pregnant women, with threatening of premature labor. In all these studies, the CL is an independent factor of PTB prediction. The threshold value with the best prediction capacity is between 25 and 30 mm and separates the high risk group from the low risk group, having a sensitivity of 60-80%[12-15]. The preterm spontaneous birth is slightly probable if the CL is ≥30 mm[14-17].

The pregnant women with painful uterine contractions (before 32 weeks) with a CL less than 15 mm have a birth risk in the next 7 days, 5.5 higher (44%), compared with those with cervical length ≥15 mm (2% risk)[13]. The data is confirmed by another study as well, where 37% of the patients with CL less than 15 mm will deliver in next 7 days from admission[14].

The reduced values (≤10 mm) of the CL were not studied separately in this group of pregnant women but the results of some studies from the general population suggest that at values of ≤10 mm there is a bigger probability that the evolution towards a preterm birth cannot be stopped. Thus, the patients with a cervix of ≤10 mm are refractory in the treatment with progesterone[18] and present increased values of the inflammation markers (cytokines, metalloproteinases)[19].

A recent meta-analysis evaluated the utility of determining the length of the cervical channel in the patients with preterm birth symptomatology[20]. Thus, for the birth up to 7 days since the admission, the negative predictive values for a cervix of 15 mm, 20 mm and 25 mm were of 94.8%, 96.3% and 95.8%.

In patients with threatening of premature labor, the transvaginal ultrasound measurement of the CL identified the women with PTB risk, has an excellent negative predictive value and helps avoiding the treatments with limited or unproven efficiency: tocolysis, hospitalization, and bed rest. At the same time, it is not clear if this determination leads to reducing the preterm birth risk.

5. Clinical applications in asymptomatic pregnant women with high risk by history of spontaneous PTB

CL has a good capacity to predict PTB in the pregnant women with a history of spontaneous preterm birth. The sensitivity and specificity of the transvaginal sonographic assessment of the CL in PTB prediction mainly depends on the cervix length and the gestational age when the measurement was made. For a threshold value of 25-30 mm, the majority of studies identify PTB before 37 weeks with a sensitivity of 60-80%, a positive predictive value of 55-70% and negative predictive value of 89-94%[21-26]. Moreover, the predictive value of a shortened cervix does not modify according to the number of prior PTB[21]. However, the gestational age when the PTB occurred affects the frequency and the speed of shortening of the cervix during current pregnancy. Thus, a precocious preterm birth (before 24 weeks) confers a higher risk of cervical shortening, characterized by a higher speed of shortening of the cervix that starts at a smaller gestational age than in the women with history of a tardive PTB (24-32 weeks)[27].

A big advantage of the ultrasound screening is that it can easily identify the pregnant women with increased risk of PTB, but who do not require treatment. In fact, over 60% of the high-risk pregnant women, such as those with history of PTB, have a CL at least 25-30 mm up to 24 weeks and do not require any intervention. Thus, the useless and expensive treatments are reduced, such as: bed rest, the transfer of the pregnant woman, administration of corticosteroids and tocolytics.

Overall, measurement of CL has highest sensitivity and positive predictive value in women with a prior PTB and a singleton pregnancy, making this population the clear favourite to potentially be associated with an effective intervention based on this screening test.

Thus, a recent analysis[28] shows that in the women with prior PTB (before 34 weeks) with the CL <25 mm, measured before 24 weeks, the cerclage of the cervix significantly prevents the PTB before 35 weeks (28.4% versus 41.3%) and the perinatal mortality and morbidity (15.6% versus 24.8%). This result is in contradiction with previous data that shows that the cervix cerclage, at the same category of women, does not prevent PTB <35 weeks unless the CL is <15 mm[29].

The vaginal administration of progesterone was studied in women with history of PTB between 20-35 weeks and shortened CL less than 28 mm at 18-22 weeks. The treatment with 90 mg vaginal progesterone up to 37 weeks was associated with a significant prevention of PTB before 32 weeks (0 versus 30%) and a significant reduction of the necessity of neonatal intensive care (15.8% versus 51.9%), compared with placebo[30]. However, although the frequency of PTB was reduced to <37, <=35 and <=28 weeks, the difference is not statistically significant, therefore these results (a secondary analysis of a larger study) must be regarded prudently.

6. Clinical applications in the general population, asymptomatic pregnant women with low risk

Women with a singleton pregnancy from general population also present a significant association between the reduction of the CL measured by transvaginal ultrasonography and PTB risk before 35 weeks[5]. Unfortunately, this relation is continuous and there is no ideal threshold of risk delimitation. Moreover, all studies present modest positive predictive values and sensitivity (19-66% and 13-20%, respectively)[3,5,31-33].

A systematic examination in general population probably represents one of the best methods of reducing the incidence of PTB if it can be associated with an efficient prophylaxis method. In the case of the cerclage, the only existent study at present ascertained that, in the general population, the cerclage of the shortened cervix less than 15 mm does not improve the obstetrical prognosis[26].

In exchange, the prophylactic use of vaginal progesterone in singleton pregnancies with shortened cervix from the general population represents one of the hopes of the current medicine. Some of these randomized studies have in common the selection of patients based on the CL measured by transvaginal ultrasonography.

The first study included patients with a CL less than 15 mm between 20-25 gestational weeks[18]. Daily vaginal administration of 200 mg of micronized progesterone reduced with 40% the PTB frequency before 34 weeks compared with the placebo group (19.2% versus 34.4%), but they did not notice a significant reduction of the neonatal morbidity and mortality. Additionally, it was proven that the patients with a cervix less than 10 mm responded much lesser to the progesterone treatment.

Afterwards, based on these results, the studies focused on the group of patients with the CL between 10-20 mm[18] with high risk of preterm birth but which can benefit at the maximum from the treatment with progesterone. Thus, the second study included patients with CL between 10-20 mm, determined at 19-24 weeks, who received daily 90 mg progesterone bioadhesive vaginal gel[34]. The analysis of the treatment intention demonstrated a significant reduction of the PTB with 45% before 33 weeks (8.9% versus 13.1%) with 50% before 28 weeks (5.1% versus 10.3%) and a reduction with 47% of the preterm children with very low birth weight (4.6% versus 13.6%) in the group treated with progesterone. Moreover, in this group,

there is a significant reduction of the respiratory distress syndrome (3% versus 7.6%) and of the composite index of neonatal morbidity.

In the end, one meta-analysis[35] that included each patient, through the aggregation of 5 high quality previous studies, ascertained that the treatment with vaginal progesterone of the asymptomatic pregnant women, with shortened cervix (≤25 mm) in the mid-trimester, reduces the risk of preterm birth before 35, 33 and 28 weeks (relative risk of 0.69, 0.58 and 0.5) and neonatal morbidity and mortality. The analysis at the patient level obtained information that can be extracted from the individual results of each study. Thus, the beneficial effect of the progesterone on PTB and neonatal morbidity was similar in different subgroups of CL (21-25 mm versus 10-20 mm versus <10 mm), but only the subgroup 10-20 mm had sufficient statistical power to be significant. The benefits of progesterone were similar both for 200 mg and for 90-100 mg progesterone and do not depend on the maternal age, the body mass index or ethnicity.

In conclusion, these key studies clearly show that the treatment with vaginal progesterone presents advantages for the women with a singleton asymptomatic pregnancy at which a reduced CL is identified.

7. Conclusion and future remarks

The determination through transvaginal ultrasonography of the CL accomplishes all the criteria of an efficient screening test of the PTB and must be part of the obstetrical practice. When performed with adequate technique, it has been shown a high objectivity and reduced inter- and intra-operative variability. Its negative predictive value allows the reduction of hospitalizations and useless treatments and the focusing towards high risk cases. Recent substantial evidence support the universal screening of the CL measured transvaginally at 19-24 weeks for all the singleton women, followed by treatment with vaginal progesterone for those with a CL less than 20 mm. The screening method is easy and in the majority of cases can be associated to the mid-trimester ultrasound screening. In the light of the new meta-analyses results, the role of the cervix cerclage must be re-assessed, being addressed to the patients that do not respond to the treatment with progesterone with a CL less than 15 mm, or those with prior PTB and a CL ≤25 mm. ■

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