Sonography of the cervix at term gestation

Madelon Meijer-Hoogeveen

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Sonography of the cervix at term gestation

Echoscopie van de cervix in de à terme zwangerschap

(met een samenvatting in het Nederlands)

Proefschrift

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Promotor: Prof. dr. G.H.A. Visser

Co-promotor: Dr. Ph. Stoutenbeek

Het is goed een doel te hebben,
maar vergeet niet onderweg te genieten

Aan mijn lieve man en dochter

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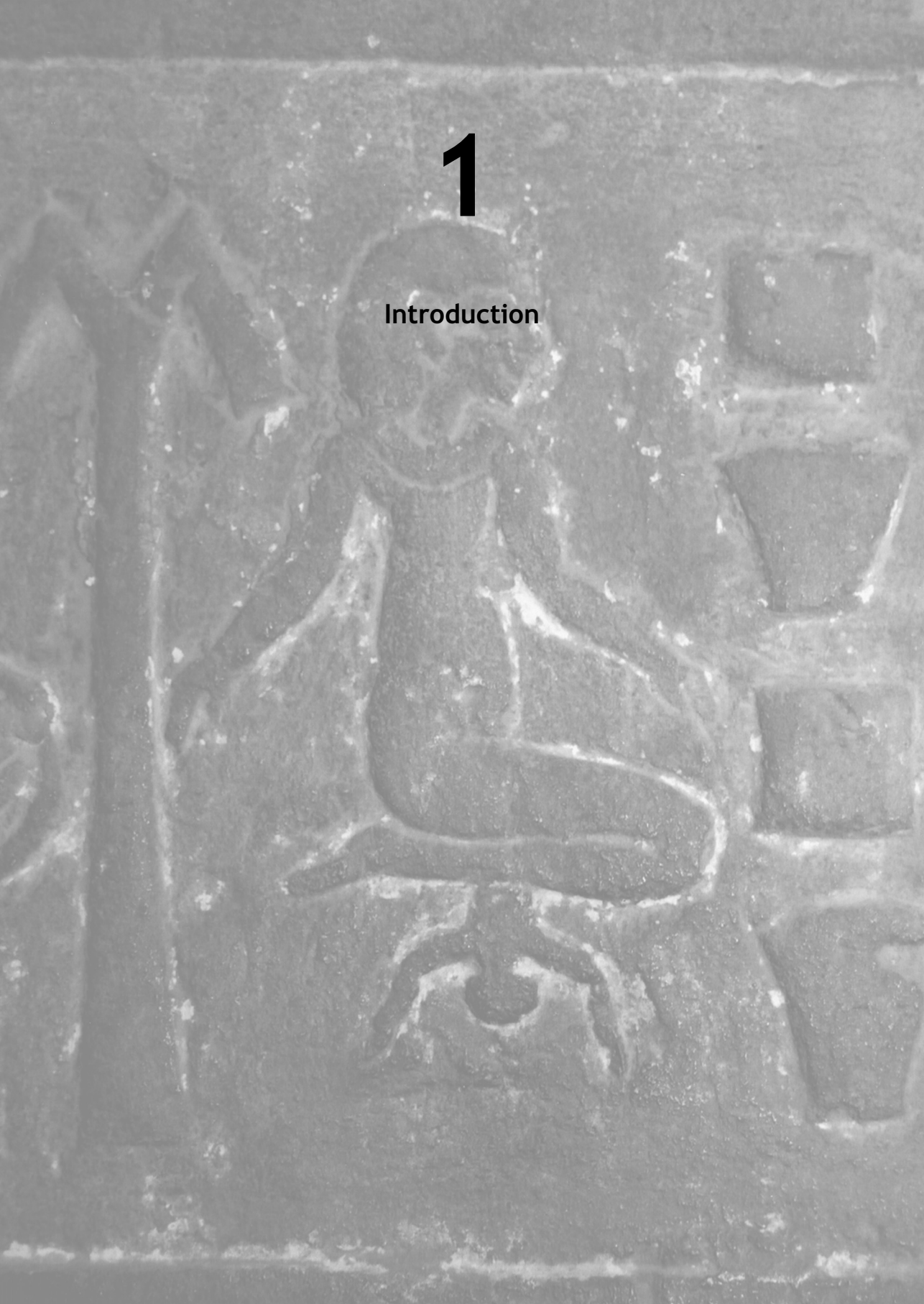

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Introduction

Introduction

The cervix consists mainly of connective tissue, containing collagen and elastin and 10-15% smooth muscle. During pregnancy the firm cartilage-like consistency of the cervix is transformed to soft tissue. A decrease in collagen concentration and an increased elastin/collagen ratio soften the rigid structure of the cervix. This transformation may be initiated long before term. This transformation is called "cervical ripening" and enables the cervix to dilate and facilitate parturition[1].

In 1960, the Bishop Score was introduced to assess cervical ripeness before induction of labour[2]. The Bishop Score is determined by digital examination, and consists of five different aspects of the cervix, namely dilatation, effacement, consistency, position and station of the presenting part of the fetus. Since then, also assessment of preterm cervical ripeness and cervical incompetence is determined by the Bishop Score.
Only recently, in the nineteen eighties, the usefulness of transvaginal sonography (TVS) of the cervix for the detection of cervical incompetence became apparent[3;4]. The advantages of TVS compared to digital examination of the cervix were recognized shortly after its introduction. Early cervical ripening, resulting in changes at the internal cervical os, can be observed by TVS, even in the absence of dilatation. Nowadays, it is considered to be reproducible[5-7] and easy to learn, even for inexperienced investigators[8]. This has resulted in a worldwide search for the optimal clinical implementation of this diagnostic tool.

TVS of the cervix is now widely used as a screening method for preterm delivery in symptomatic and asymptomatic women. Women with symptoms of preterm labour benefit most from screening by TVS. When cervical length (CL) on TVS is shorter than 15mm, 40-47% of these women will deliver within 7 days, irrespective of the use of tocolysis. In contrast, a CL ≥15mm is reassuring since less than 1-2% will deliver within 7 days[9;10].
In asymptomatic women, TVS of the cervix is most beneficial for the identification of women at low risk for preterm delivery[11]. However, a short cervix at mid-gestation ultrasound does increase the risk of preterm delivery in this group. Although cut-off points vary between different studies, a CL smaller than 25mm is the most commonly used threshold to detect women at risk for preterm delivery (OR 4.40; 95% CI 3.53;5.49)[12]. A cerclage may prevent preterm delivery, especially in women with a history of cervical incompetence or preterm delivery[13]. When a CL smaller than 25mm is found in women at high risk for preterm delivery, a cerclage in combination with bed rest may decrease the prevalence of preterm delivery compared to bed rest alone. In one Dutch study the prevalences were 44 and 1% respectively[14]. A shorter cut-off for CL probably identifies women at high risk more accurately, but may increase the risk of ascending infection after the procedure[15].

In the latest two decades, the clinical use of TVS of the cervix has further been expanded. There was need for a way to predict the outcome of labour induction at term more accurately than by the Bishop Score. In several studies pre-induction assessment of cervical ripeness by TVS has been compared with digital examination, but so far results are conflicting.

It is striking that with the rapid evolvement of TVS in general clinical practice, only a few small studies report on physiological changes of the cervix preceding term labour. Knowledge of the physiology of the cervix at term is necessary to interpret TVS results in case of threatened preterm labour or before induction of labour at term.

Aim and outline of the thesis

It is the general objective of this thesis to study the cervix by TVS at term to obtain more insight in physiological changes preceding parturition, and to relate these changes or otherwise to the onset and course of spontaneous labour and to the need for and outcome of induced labour.

This thesis aims to answer the following questions:
1-What is the "gold standard" to obtain optimal cervical measurements by real time ultrasound, which are the pitfalls and what is the relevance of the different cervical parameters? This is addressed in a literature review (*chapter 2*).
2-What are the fluctuations in CL and which factors cause fluctuations? This was studied by performing continuous TVS of the cervix for 30 minutes (*chapter 3*).
3-How reliable are transperineal CL measurements at term gestation? In case of preterm rupture of the membranes (PROM) or reluctance with transvaginal examination it may be relevant to have a reliable substitute for the transvaginal approach. Literature has shown that transperineal CL measurements can be used reliably during the preterm period. We have investigated this at term (*chapter 4*).
4-Which are the cervical changes that precede spontaneous onset of labour at term and can the timing of labour be predicted by CL measurements? This was studied in a homogenous nulliparous population by serial TVS of the cervix from 36 weeks of gestation onwards (*chapter 5*). Furthermore, the effect of a maternal postural change (from supine to upright position) on the predictive value of the CL measurements was studied.
5-Do pre-induction CL measurements in either supine or upright position predict the outcome of labour induction at term better than the Bishop Score? Previous studies on the prediction of success after labour induction appear to be contradictive (*chapter 6*).
6-Can TVS of the cervix or the Bishop Score predict spontaneous onset of labour beyond 41 weeks of gestation? This might be helpful in the decision for either induction of labour or expectant management at prolonged pregnancy. We studied nulliparous women, who have a higher risk of failed induction than parous women (*chapter 7*).
7-Can women at high risk for a repeat caesarean section (CS) be detected by CL measurements? For this purpose we studied women with a previous CS for failure of progress or breech presentation. Serial TVS of the cervix was performed from 36 weeks of gestation onwards (*chapter 8*), in order to detect differences between women who delivered vaginally and those who needed a repeat CS.

In *Chapter 9* the results are summarized and recommendations for clinical use are given.

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2

Methods of sonographic cervical length measurement in pregnancy: a review of the literature

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Philip Stoutenbeek
Gerard H.A. Visser

Abstract

In this review we give an overview of the methods and pitfalls in cervical length measurements. We compared the different techniques and investigated factors that influence visualization of the cervix. The data of this overview may be used to establish guidelines in clinical practice.

Introduction

Sonography of the cervix in pregnancy has been subject to a rapid development, since its introduction in the nineteen eighties. Initially, abdominal scans were performed to diagnose cervical incompetence. The following three decades intensive research has been done to investigate the behaviour of the cervix and the ability to predict preterm labour by cervical measurements. Normal ranges of the cervical length (CL) throughout pregnancy in singleton and multiple pregnancies have been published[1-13]. Young age, low prepregnancy BMI and Asian, Afro-Caribbean or African ethnicity have been reported to be correlated with a shorter CL[14-18]. The significance of funneling in predicting preterm labour has been studied, and provocation of funneling has been tested by different techniques. Recently, there has been a shift of interest towards the term period, where the cervix has been investigated in predicting the success of induction of labour.
Previous review articles[19-29] have evaluated the predictive value of CL measurements with only limited attention towards methodological considerations. The aim of this review is to give an overview of the methods and pitfalls of sonographic CL measurement in pregnancy. The data of this overview may be used to establish guidelines in clinical practice.

Literature search

In this review, we compare the different techniques and investigate factors that influence visualization of the cervix. For this purpose we searched Pubmed for English literature on "cervical length" and "pregnancy". This resulted in 595 references and 56 review articles.
To complete our search for methods in CL measurement, we added the following search terms: "transvaginal ultrasound", "funneling", "twin", "triplet", "transperineal", "translabial", "maternal position", "standing", "transfundal pressure", "three dimensional", and "contrast agent". As a next step, we selected the literature and references that compared different techniques to visualize the cervix. Studies that investigated only CL cut-off points for predicting preterm labour or the need for a cerclage, studies on non-pregnant women, and studies investigating only the predictive value of the cervix for successful induction or spontaneous term labour were excluded. As a result, 73 original articles and 11 review articles were selected for this review.

Transabdominal, transvaginal or transperineal cervical length measurement?

When the cervix first became object of interest, investigators and clinicians promptly encountered the limitations of the abdominal scan. Especially with advanced pregnancy, the cervix is obscured by the fetal head, and visualization of the complete cervical canal is difficult. Furthermore, a short cervix or an empty bladder both reduce the quality of the

CL measurement in the midtrimester[18], whereas a full bladder may artificially lengthen the cervix[30;31]. To et al[18] reported that a clear transabdominal image of the cervix could only be obtained in 73% of patients with a full bladder, and in 49% after voiding, at 23 weeks of gestation. Identification of the internal and external os improved with increasing CL. To improve the reliability of CL measurements, the transperineal and transvaginal methods were investigated.

Initially, transperineal scanning of the cervix appeared to be a feasible alternative when compared with transabdominal ultrasound[32]. Particularly when transabdominal imaging of the cervix is difficult in the third trimester of pregnancy, the cervix can be well visualized by the transperineal method[33]. However, some disadvantages limit the utilization of this technique. The external os of the cervix can be obscured by bowel gas or shadowing from the pubic symphysis[34]. Failure of visualizing the complete cervical canal has been described in 3-12% of the cases[35-39], and appeared to be dependent on the experience of the investigator[35;36;40]. A generous amount of ultrasound gel[32], oblique rotation of the transducer[39] and elevation of the hips[41] have been reported to improve the transperineal image of the cervix. In the elevated hip position, the bowel is removed from the cul-de-sac, and the cervix is imaged at a steeper angle.

The transvaginal method is less dependent on gestational age, and a clear image of the cervix can be obtained in nearly 100% of the cases. It is considered reproducible[42-44], and easy to learn, even for inexperienced investigators[45]. Currently, the most common method to measure the cervix is transvaginal, with the patient in supine position with an empty bladder. Pressure on the cervix with the transducer should be avoided[46], since this can artificially lengthen the cervical canal. In case of curvature of the cervix, the cervix is on average measured longer when the cervix is measured along the curvature than when it is measured in a straight line (Figure 1)[47]. However, this difference is more pronounced in the longer cervix, and therefore clinically irrelevant. Measuring the CL in a straight line is advised to improve the reproducibility of the measurement. Although the transvaginal method is now considered the "gold standard", it may not always be possible or preferred, e.g. in case of premature rupture of the membranes (PROM). In search for a reliable substitute for transvaginal scanning of the cervix, the transperineal method again appears to be the most feasible alternative.

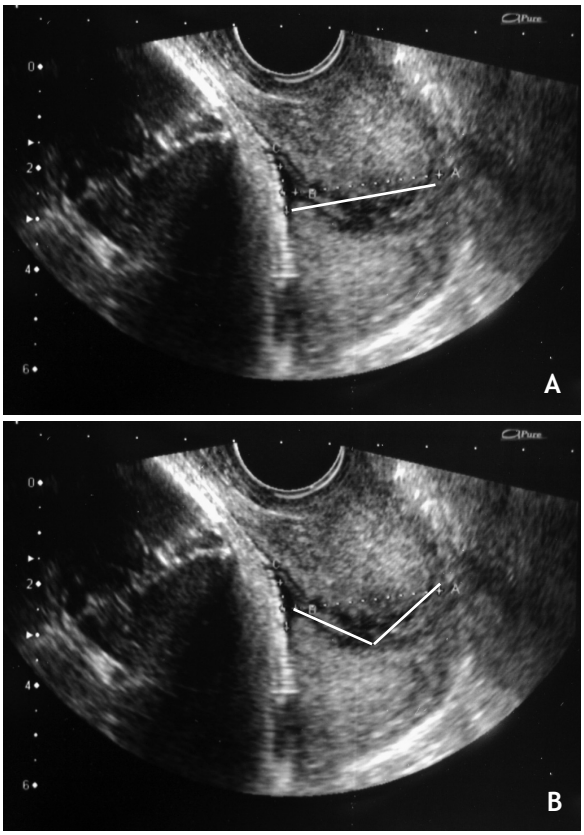

Figure 1: CL measurement in a curved cervix. The cervix can be measured in a straight line (A) or along the curvature (B).

The transperineal approach has been reported to correlate reasonably well with transvaginal measurement of the cervix, with correlation coefficients ranging from 0.77 to 0.97[35;38-40;48;49] (Table I). Owen et al[36] reported a deviant correlation coefficient of 0.38 and a difference between the two methods of 20% or more in one third of the cases. They concluded, that the transperineal approach is only a reliable substitute for the transvaginal method in centres with extensive experience, which is in agreement with the conclusion made by Cicero et al[35]. In the latter study, the transperineal approach was compared to transvaginal examination of the cervix in two phases. In the initial learning phase of the study, 200 patients were examined. Afterwards, the transperineal images of the cervix were reviewed, and it became apparent that more than 50% of the images were inadequate due to shadowing. In the second phase of the study, reliable images could be obtained in 78% of the cases, when special attention was paid to visualizing the internal and external os.

Since transvaginal images of the CL can be obtained in nearly 100% of the cases and since this method is less dependent on gestational age or the experience of the investigator, it should remain "the gold standard". Transperineal scanning of the cervix may be used as an alternative for patients with PROM, when transvaginal investigation is undesirable, or in case of a psychological reluctance with vaginal examination.

Table I: Transvaginal (TV) versus transperineal (TP) CL

Study characteristics

Author	*Nr*	*GA*	*Object*	*Position*	*Experience*	*Failure*	*Mean diff (range mm)*	*Correlation*
Berghella et al.1997	1110	18-25	Funneling	Supine		0%		0.82
Kurtzman et al. 1998	206	14-34	CL Funneling	Elevated hips or stirrups	100 TP scans	0%	1 (-5.7;4)	0.95
Owen et al. 1999	102	15-24	CL Funneling	Supine	>10 years TV	11%	1.6 (-19;27)	0.38
Carr et al. 2000	84	14-40	CL	Supine	3 years TP	5%	5 (1;23)	0.77
Cicero et al. 2001	300	22-24	CL	Supine	>2000 TV / 65 TP scans	12%	0.2 (-5.8;6.1)	0.93
Yazici et al. 2003	357	24	CL	Elevated hips		11%		0.83
Ozdemir et al. 2005	36 32 33	10-14 20-24 30-34	CL Funneling	Elevated hips		3% 0% 0%	2.8 ± 2.3 0.9 ± 1.3 0.5 ± 1.4	0.93 0.97 0.97

Presence of funneling

Funneling is defined as herniation of the fetal membranes into the cervical canal. Although funneling is in general considered to be a sign of cervical insufficiency and therefore a risk factor for preterm delivery, there is not yet consensus about how to measure the funnel. Zilianti et al[50] described the different shapes in funneling. The letters T, Y, V and U mark the successive stages of effacement from absent to extensive (Figure 2). The predictive value of these levels of funneling for the prediction of preterm labour still remain unclear.

Attempts have been made to standardize funneling. Funneling can be expressed in funnel width, funnel length and as a percentage of the cervical canal. However, the shape of the funnel often varies during investigation[51], and therefore measuring the funnel might be inappropriate and falsely suggest precision. Recording the presence of a funnel in combination with the shortest measurement of the cervical canal is most representative of the functional status of the cervix[19].

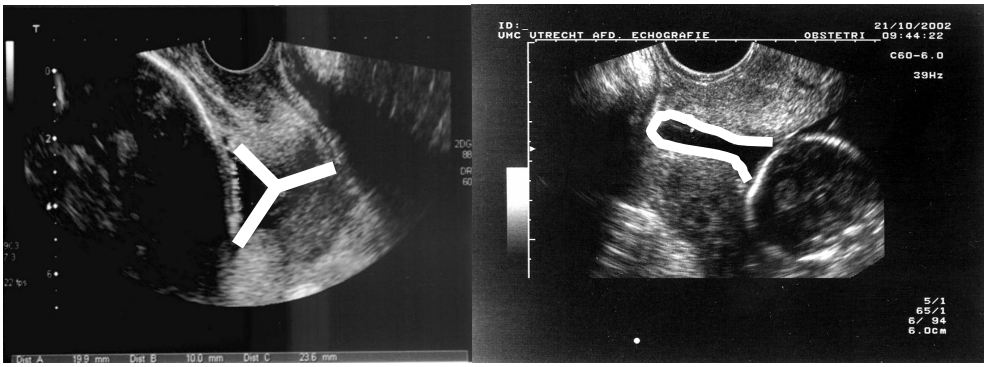

Figure 2: Examples of Y (left) and U (right) shaped funneling. Successively the letter T represents the absence of funneling, the letter Y the first stage of funneling, and the letters U and V represent a funnel extending over the complete cervical canal.

Does the presence of a funnel add to the CL measurement in predicting preterm delivery? Bergelin et al[12;13] observed the presence of funneling long before term delivery in both nulliparous women and parous women from 30 and 24 weeks of gestational age onwards, respectively. In these cases the residual CL appeared to be a better predictor of preterm delivery than the presence of funneling. In addition, in Chinese nulliparous women who delivered at term, funneling was present in 25% of the cases, with the earliest appearance at 36 weeks of gestation[52]. Funneling was not correlated to the gestational age at delivery. A study comparing singleton and twin pregnancies with threatened preterm labour showed funneling more frequently in twin pregnancies between 23 and 33 weeks of gestation[53]. In both singleton and twin pregnancies the presence of funneling was unable to predict birth before 34 weeks of gestation. When preterm birth was defined as birth before 37 weeks of gestation, the presence of funneling was predictive in singleton pregnancies. However, CL was the only independent predictor of preterm delivery in this study. When routine examination is performed in the midtrimester, the presence of funneling is observed in a small percentage of the population, and appears to have no additional value over the measured residual CL in the prediction of preterm delivery, nor in high risk[54;55] nor in low risk patients[56;57]. However, in four recent studies funneling was found to be an independent predictor of preterm delivery. Rust et al[58] examined women with a short cervix -smaller than 25mm- in the midtrimester, and matched for funneling or no funneling. They found that the presence of funneling significantly increased the risk for preterm delivery that was based on CL. Leung et al[59] found that the presence of funneling was a significant independent predictor for preterm delivery before 34 weeks of gestation, but not for before 37 weeks of gestation. De Carvalho et al[60] considered funneling present when it consisted of at least 25% of the entire CL. In only 1.5% of the women examined at 21-24 weeks of gestation funneling was present; however, there was a strong independent correlation with preterm

birth before 34 weeks of gestation. In 65 women with twin pregnancies, Yang et al[61] found that the presence of any funneling was a significant independent predictor of early preterm birth before 32 weeks of gestation.

To estimate the odds ratio (OR) for preterm delivery before 35 weeks of gestation when funneling is present before 34 weeks of gestation, we selected prospective cohort studies that reported the exact numbers of preterm labour in the presence and absence of funneling[53;54;56;59;62]. The study population was considered "high risk" when there was a history of preterm delivery before 32 weeks of gestation, or when the present pregnancy was complicated by symptoms of preterm labour or cervical shortening (Table 2). Funneling was present in 4-6% of the low risk populations, compared to 9-19% of the high risk populations. In the low risk populations 1% delivered preterm, compared to 7-26% in the high risk populations. The weighted OR for preterm delivery in the presence of funneling is 5.61 (95% CI 4.40;6.82) in a high risk population and 9.44 (95% CI 8.30;10.58) in a low risk population (Figure 3). The higher OR for preterm delivery in the low risk population compared to the high risk population can be explained by the low a priori risk for preterm delivery and the low prevalence of funneling in the low risk population. It has to be noted, however, that we were not able to correct these data for the actual CL.

The presence of a funnel appears to be physiologic during the third trimester of pregnancy, but seems an independent predictor of early preterm birth when present in the midtrimester. However, the exact criteria for funneling still remain unclear.

Table 2: Risk of preterm delivery (PD) in the presence of funneling

Author	*Observation period (GA)*	*Funneling absent**		*Funneling present**		*Definition preterm labour*
		PD-	*PD+*	*PD-*	*PD+*	
		HIGH RISK				
Owen 2001	16-24	129	38	7	9	GA<35
Crane 1997	23-33	115	5	12	4	GA<34
Andrews 2000	16-29	101	21	13	16	GA<35
		LOW RISK				
Leung 2005	18-22	2686	13	175	6	GA<34
To 2001	22-24	6060	43	215	16	GA<33

***Number of patiens as reported in the data of the selected studies.**

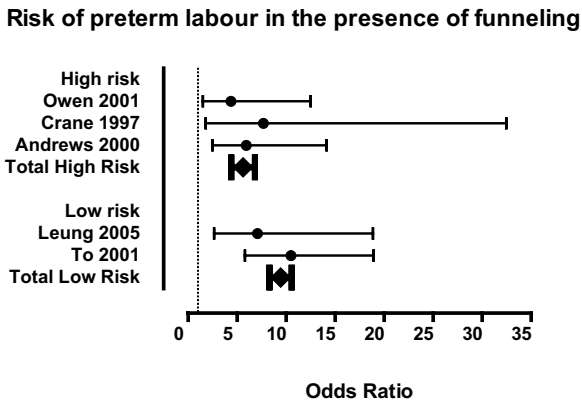

Figure 3: Meta-analysis of the risk of preterm labour in the presence of funneling.

Provoking cervical insufficiency by transfundal pressure and standing

Transvaginal sonography (TVS) of the cervix is being used to detect cervical insufficiency, which is defined as shortening of the CL and herniation of the fetal membranes into the cervical canal. These changes of the internal cervical os may vary with time, and therefore cervical insufficiency may be masked[51;63].

Initially and in a small study, Guzman et al[64] tried to provoke funneling by transfundal pressure. Thirty-one pregnant women at risk for cervical incompetence underwent TVS. In fourteen women, who initially had a normal appearance of the cervix, there was funneling present after transfundal pressure for 15 seconds. In two more women cervical changes were only detected on subsequent evaluations. In a normal control group, consisting of 150 women between 16 and 24 weeks of gestation, the cervix did not change in response to transfundal pressure. Two other studies in women at high risk for preterm delivery showed that transfundal pressure could elicit cervical shortening in the mid-trimester, and that on successive ultrasound examinations, this shortening was progressive[65;66].

Since transfundal pressure is difficult to standardize, investigators have tried to provoke cervical incompetence by several other methods. Wong et al[67] investigated 41 high risk women between 17 and 33 weeks of gestation in supine and upright position, both after 15 minutes, for cervical incompetence. They found that either a CL less than 20mm or a postural change in CL of 33% or more was associated with a delivery before 37 weeks with a sensitivity of 100% and a specificity of 92,3%. Another study compared the method of a postural change with transfundal pressure and coughing[68] in the midtrimester. The method of transfundal pressure had the highest sensitivity and specificity 83,3% and 95,8%, respectively. In the upright position the cervix was evaluated after 1 minute, which might account for the difference as compared to Wong et al[67], who evaluated the cervix 15 minutes after the postural change. A lack of difference in CL between the supine and upright position was also found by Meath et al[69]. TVS was performed weekly between 17 and 34 weeks of

gestation in 12 singleton, 13 twin and 7 triplet pregnancies, and preterm birth rates were 25%, 77% and 100% respectively. They were not able to detect a clinical significant reduction in CL in the upright position or during the Valsalva maneuver.
In normal control patients, no significant changes between the supine and upright position have been found before 25 weeks of gestation[70], which is in agreement with the findings based on transfundal pressure[64]. After 35 weeks of gestation, significantly more funneling occurred in the upright than in the supine position, which might be due to a physiological destabilization of collagen in the cervix[70]. These alterations in the physiology of the cervix have been observed both in singleton and in multiple pregnancies. In women with twin pregnancies who delivered after 36 weeks of gestation funneling has been found in the upright position from 30 weeks onwards[71].
Pseudodilatation of the cervix based on lower uterine segment contractions has been observed before 35 weeks of gestation[72]. The amniotic cavity can be narrowed by a contraction, and therefore mimic funneling. In addition, a mucus plug can erroneously be regarded as a funnel. Pseudodilatation of the cervix must be considered when 1) a contraction is visible in the myometrium, 2) the cervix appears longer than 50mm, and 3) the cervical canal appears to be caudal to the funnel.
When a patient is at risk for preterm delivery, a transvaginal image of the cervix made with the patient in supine position between 25 and 35 weeks of gestation, may mask the insufficient cervix. To avoid missing the diagnosis of cervical incompetency, clinicians should perform one of the provocation techniques when the cervix appears normal in supine position. Funneling at provocation is only of significance before 35 and 30 weeks of gestation, respectively in singleton and twin pregnancies. Thereafter it should be considered physiological.

Prospectives: use of contrast agents in assessing cervical length

The most common difficulty that is encountered during cervical measurements is the appearance of shadow obscuring the external os. Both intravaginal saline and methylcellulose gel have been used to improve the image of the cervical canal. In 26 patients in the midtrimester, saline infusion in the vagina most commonly revealed a shorter CL than estimated before saline infusion, with differences between 3 and 11mm[73]. The identification of funneling was not different before and after saline infusion. Furthermore, intravaginal saline infusion improved the image of the cervical canal in 6 patients with inadequate transabdominal visibility of the cervix[74]. In the term period, preinduction identification of the cervix improved with intravaginal saline infusion[75].
Theoretically, methylcellulose gel is a better contrast agent than saline, due to its viscosity. Intravaginal methylcellulose gel improved the transperineal image of the cervix in 17 out of 25 patients in the midtrimester, versus 6 out of 25 patients who received intravaginal

saline[76]. However, in this study CL was not significantly different before and after either contrast agent.
The use of contrast agents appears to be a feasible aid to obtain an image of the complete cervical canal. Further investigation is necessary to estimate the risk of infection and to improve the method of infusion.

Prospectives: 3D ultrasound assessment of the cervix

With conventional TVS a midsagittal image of the cervix is obtained to measure the cervical canal. Examination of the cervix in an oblique plane may cause under- or overestimation of the CL. 3-D sonography may add to a more complete and accurate image of the complete cervical canal[77].
A comparison between 2-D and 3-D TVS of the cervix most commonly reveals a difference in CL of +/- 5mm or more[77-79]. The largest differences in CL between the two methods have been observed when the cervix is longer than 30mm[79], which is clinically irrelevant. Funneling is detected more often by 3-D ultrasound, suggesting that a funnel is not always perfectly cone-shaped[77;78].
Hoesli et al[80] compared 2-D CL and 3-D volumetry of the cervix in high and low risk patients for preterm delivery. They observed a good correlation between 2-D and 3-D measurement of the cervix, however the 2-D measurement was more distinctive between the two groups. When the two methods were compared in a high risk group with CL ≤25mm the 3-D measurement of the cervix appeared to have a better positive predictive value (PPV) for preterm delivery than conventional 2-D sonography[81]. In a comparison between abdominal 2-D and 3-D sonographic determination of the cervix in higher order multiple gestation, 3-D scans only provided additional information when conventional 2-D measurements were unobtainable[82].
Furthermore, 3D power doppler ultrasound of the cervix has been used to detect changes in vascularization of the cervix that might reflect the ripening process[83;84]. Intraindividual changes in cervical flow appeared very small and not helpful in predicting preterm delivery or labour induction.
Theoretically, 3-D ultrasound provides a more accurate and complete image of the cervix than conventional 2-D ultrasound. However, the clinical usefulness of this technique seems limited and may need further investigation.

Guidelines for cervical measurement

The "gold standard" is a transvaginal scan, with the women in supine position, after emptying the bladder. Pressure of the transducer on the cervix should be avoided. In case of curvature of the cervix, it is measured in a straight line.

When TVS of the cervix is undesirable, such as in case of PROM, transperineal ultrasound is the best alternative at least in the hands of experienced investigators.
The functional status of the cervix is best reflected by recording the shortest CL, and merely the presence of funneling. Attempts to measure the funnel falsely and inappropriately suggest precision. Funneling present in the midtrimester appears to be a predictor of early preterm birth, although the exact criteria for funneling still remain unclear. Funneling can be masked in the supine position, and therefore provocation of cervical insufficiency by transfundal pressure and/or standing is recommended. During the third trimester of pregnancy funneling seems physiological. Lower uterine segment contractions may mimic the presence of a funnel, but in these cases generally a long CL will be found.
Theoretically, 3-D ultrasound provides a more accurate and complete image of the cervix than conventional 2-D ultrasound, since 2-D examination of the cervix in an oblique plane may cause under- or overestimation of the CL. Future investigations will demonstrate the clinical usefulness of this technique

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3

Dynamic cervical length changes; preliminary observations from 30 minutes transvaginal ultrasound recordings

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Abstract

Objective The purpose of this study was to visualize and quantify dynamic changes in the cervix and to study factors influencing cervical length (CL).

Methods Eighteen women with a gestational age between 23 and 40 weeks were examined by transvaginal ultrasound during a continuous observation period of 30 minutes.

Results All women delivered beyond 34 weeks of gestation, fourteen at term. The overall mean difference between the shortest and longest CL during the 30 minutes recordings -CL variation- was 10.9mm (range 1.6-26.7mm). In the presence of fetal movements directed at the cervix, peristaltic movement of the bowel or contractions, CL variation was larger than in the absence of these conditions (mean 12.7mm; range 5.2-26.7mm and mean 6.1mm; range 1.6-9.4mm, respectively; P=0.03).

Conclusions Dynamic changes in CL are present at early gestation and long before delivery and can be observed either spontaneously or associated with contractions, fetal movements or peristalsis. These conditions must be considered as pitfalls in CL measurement. In critical cases, such as early threatened preterm labour, increase of the frequency and duration of sonographic ultrasound measurements may be helpful to obtain a more reliable estimation of the cervical status.

Introduction

Sonographic estimation of the cervical length (CL) is widely used to predict preterm birth, either in pregnancies complicated by threatened preterm labour, or as screening in high or low risk populations. With such measurement it is assumed that the CL does not vary with time. However, changes in CL have been observed by several research groups. It has been suggested that observation of the cervix for 5 minutes is likely to detect possible changes in CL, and that the shortest measurement is most likely to predict preterm birth[1]. Moreover, adding transfundal pressure or a postural change to the examination can detect cervical insufficiency that would otherwise remain masked in the supine position[2]. Artificial changes can be observed when pressure is exerted on the transvaginal ultrasound probe[3], or when the bladder is full[4;5], both resulting in an elongation of the cervical canal. Furthermore, contractions of the lower uterine segment can alter the appearance of the cervix[6]. Spontaneous changes in CL have also been observed in the absence of contractions[7-9]. However, the significance of these dynamic changes remain unclear.
The aim of this study is to visualize and quantify dynamic changes in the cervix during a continuous observation period of 30 minutes, and to study factors influencing CL measurement.

Materials and Methods

In a one-year period between June 2005 and June 2006, women who attended the outpatient clinic for a CL measurement were asked to participate in the study. All women who agreed to participate gave informed consent. At a subsequent visit, the cervix was observed during a continuous 30 minutes period, with the women in supine position. The examinations were performed with a 6-MHz transvaginal probe (APLIO, Toshiba Medical Systems, Tokyo). Care was taken to avoid pressure on the cervix and to maintain a sagittal plane of the cervix with a clear image of the internal and external os and the complete cervical canal. Before start of the observation period women were asked to empty the bladder. During the 30 minutes observation, presence or absence of contractions were monitored by a tocograph (Hewlett Packard 8040A, Boeblingen, Germany). The CL was observed continuously, and CL measurements were taken when alterations in the appearance of the cervix were observed. Fetal movement and peristalsis were observed during the ultrasound examination. Fetal movement was considered present when movements of the fetal head or limbs were observed on transvaginal ultrasound. Peristalsis was considered present when peristaltic movement of the bowel was visible within the scanning range of the transvaginal probe.
All examinations were performed by a single sonographer (M.M.) and recorded on tape for further analysis. Significant alterations in the appearance of the cervix were reviewed by

an experienced sonographer (Ph.S.). Clinicians were blinded to the 30 minutes ultrasound findings, to avoid clinical management being influenced.
Statistical analysis was performed with SPSS 12.0. The Pearson correlation was used to determine the correlation between CL variation and both gestational age (GA), ultrasound-delivery interval and amount of peristaltic movement. An unpaired t-test was used to assess the difference in CL variation between patients. P values <0.05 were considered statistically significant.

Results

Eighteen women with a GA between 23 and 40 weeks participated in the study (Table 1). In all but one of the woman the observation period lasted 30 minutes. One women (patient 3, GA 35^{+2}) was not able to remain in supine position for 30 minutes and the examination was discontinued after 15 minutes. Six were nulliparous women. Five of the twelve multiparous women had a previous preterm delivery and were considered at high risk for preterm delivery. Of these women, 2 used hydroxyprogesteron in the current pregnancy (patient 14 and 18). One more high risk multiparous woman (patient 16) was admitted to the hospital for threatened preterm labour at 28 weeks of gestation, and had received tocolysis for 24 hours when the 30 minutes observation of the cervix was performed. There were no contractions observed by tocography or reported by the patient during the observation period. This patient delivered spontaneously at 34^{+3} weeks of gestation. All other women delivered beyond 36 weeks of gestation in the current pregnancy, except one, who had a caesarean section on maternal indication at 35 weeks of gestation. The overall mean GA at delivery was 38^{+6} weeks, range 34^{+3} to 42^{+4} weeks.

Table 1: Patient characteristics

Patient	*GA 30 min recording (weeks)*	*Longest CL (mm)*	*Shortest CL (mm)*	*CL variation (mm) = long-short CL*	*CL variation (%) = Diff/mean*100*	*GA delivery (weeks)*	*Video-delivery interval (weeks)*
NULLIPARAE							
1	24^{+6}	35.6	26.4	9.2	26	40^{+6}	16
2	30^{+1}	39.3	12.6	26.7	68	37^{+6}	7^{+5}
3	35^{+2}	43.6	42.0	1.6	4	39^{+6}	4^{+4}
4	37^{+2}	45.3	32.3	13.0	29	42	4^{+5}
5	38^{+5}	41.4	28.9	12.5	30	39^{+5}	1^{+1}
6	40^{+1}	12.9	5.7	7.2	56	41^{+2}	1^{+1}
MULTIPARAE LOW RISK							
7	28^{+1}	46.3	41.1	5.2	11	42^{+4}	14^{+3}
8	29^{+6}	47.4	36.4	11.0	23	35^{+1} *	5^{+2}
9	30^{+5}	43.5	38.7	4.8	11	40^{+5}	10
10	31^{+2}	48.8	37.6	11.2	23	39^{+1}	7^{+6}
11	35^{+1}	60.9	49.1	11.8	19	40^{+3}	5^{+2}
12	36^{+2}	48.0	36.2	11.8	25	37^{+5}	1^{+3}
MULTIPARAE HIGH RISK							
13	23^{+3}	44.5	33.5	11.0	25	36^{+2}	12^{+6}
14	24^{+1}	51.7	29.7	22.0	43	39^{+4}	15^{+3}
15	26^{+6}	36.4	21.1	15.3	42	37^{+6}	11
16	28^{+0}	16.8	11.3	5.5	33	34^{+3}	6^{+3}
17	30^{+3}	39.1	32.3	6.8	17	37	6^{+4}
18	30^{+4}	28.2	18.8	9.4	33	36^{+2}	5^{+5}

* Maternal indication

The overall mean shortest CL measurement was 29.7mm (range 5.7-49.1mm). The overall mean difference between the shortest and longest CL during the 30 minutes recordings -CL variation- was 10.9mm (range 1.6-26.7mm), and was most pronounced in patient 2 and patient 14 (26.7mm and 22.0mm, respectively). The mean ultrasound-delivery interval was 54 days (range 8-112 days). There was no correlation between the CL variation and the gestational age at the 30 minutes observation (Pearson correlation -0.20; P=0.43; 95% CI -0.54;0.39), or with the ultrasound-delivery interval (Pearson correlation 0.16; P=0.52; 95% CI -0.33;0.58). The CL variation of individual patients is shown in figure 1-3.

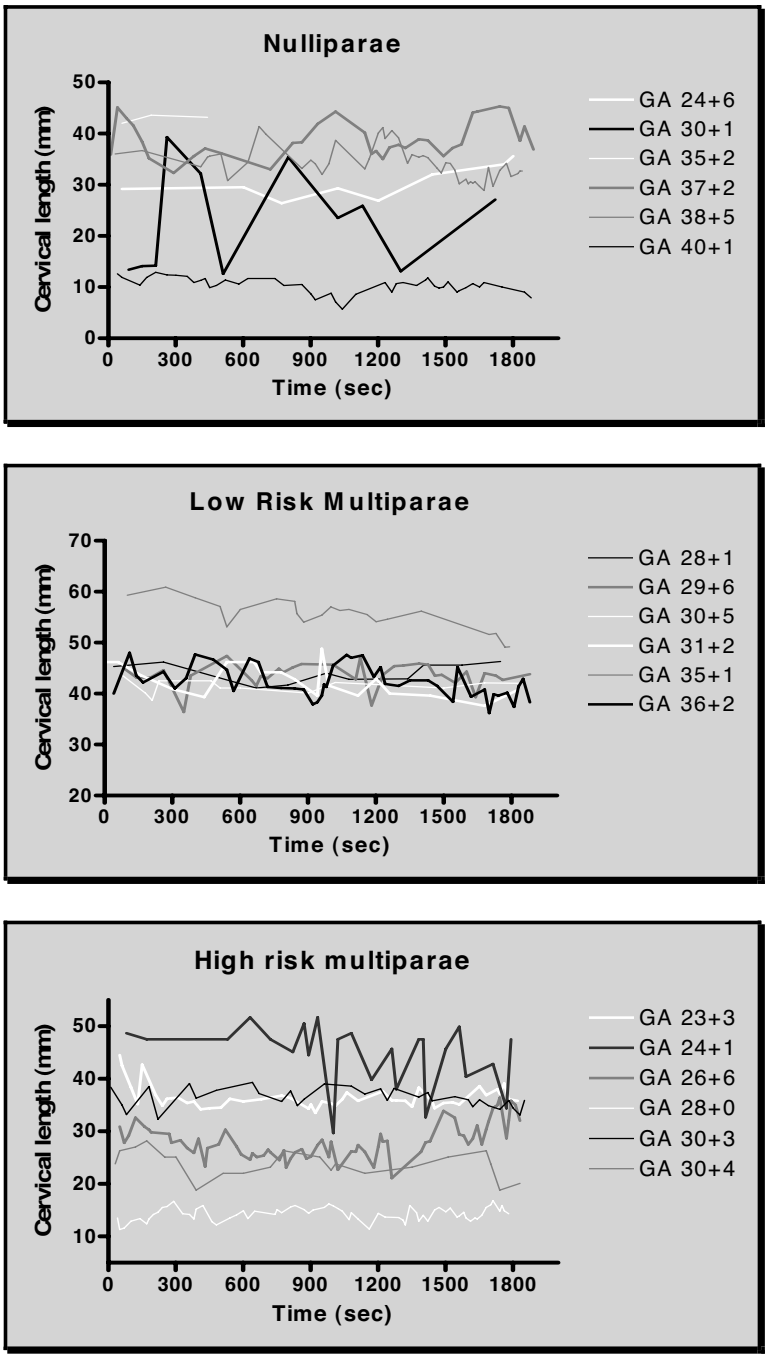

Figure 1-3: CL variation during a continuous 30 minutes period in nulliparous, low risk and high risk multiparous women respectively.

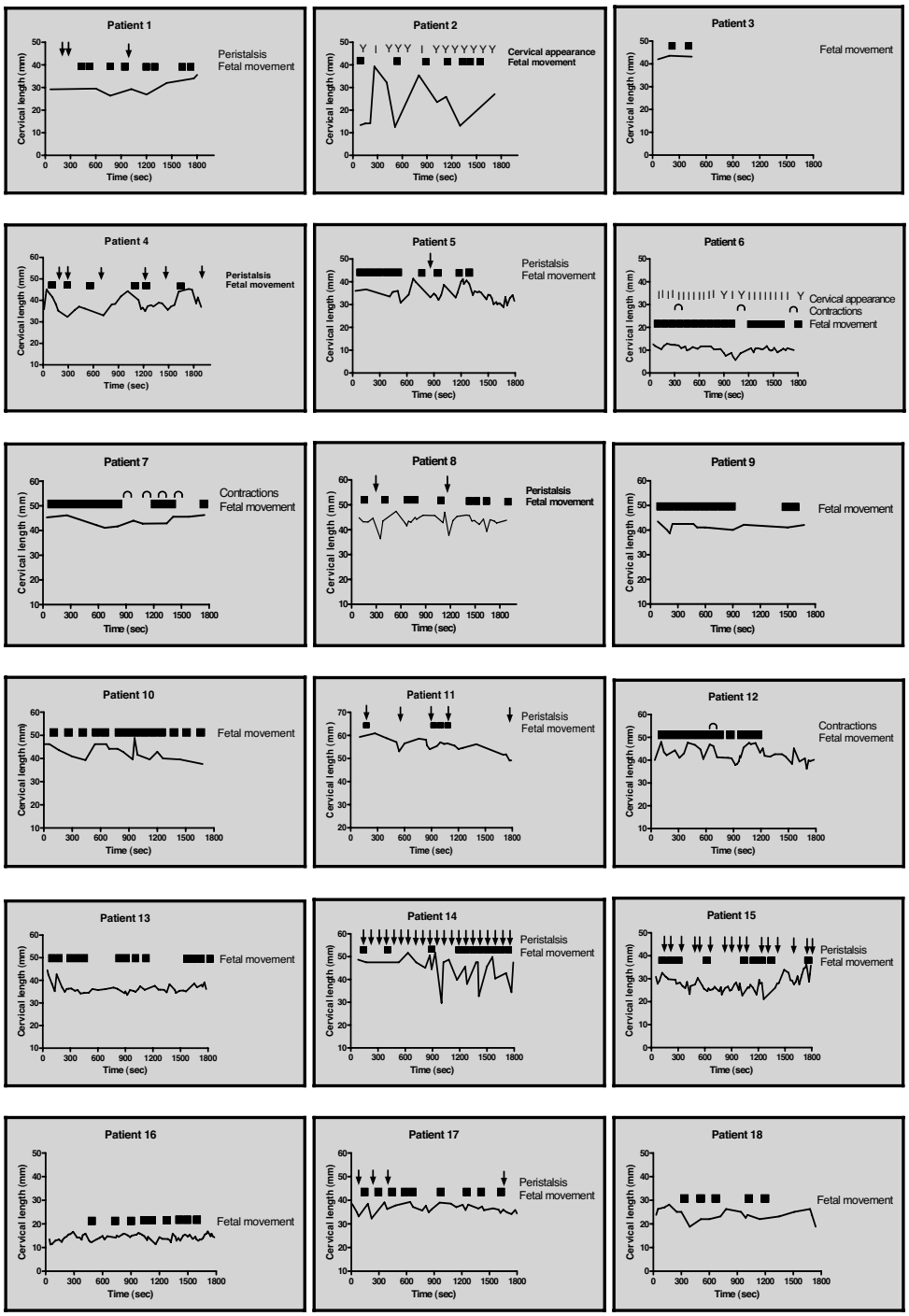

Figure 4: CL variation in individual patients. Fetal movement is indicated by squares, peristalsis by arrows, contractions by arcs, and in patient 2 indicate Y and I respectively the presence and absence of funneling

Patient 2 (figure 1, GA 30^{+1}) had a cervix that varied during the observation period between 36.3mm and 12.6mm based on spontaneous opening and closure of the internal os, thus funneling, being alternately present and absent. Previously, at 28 weeks of gestation, this nulliparous woman had been admitted for threatened preterm labour and received tocolysis. She was discharged at 29 weeks of gestation, and attended the outpatient clinic for a 30 minutes CL measurement at 30 weeks of gestation. Fetal movements were associated with variation in the appearance of the cervix (Figure 4, patient 2). However, spontaneous opening and closure of the internal os was observed in the absence of fetal movements. No contractions were recorded by the tocograph nor reported by the patient during the observation period. The gestational age at spontaneous onset of delivery was 37^{+6} weeks.
In two other patients with a cervix shorter than 15mm (Figure 4, patient 6 and 16), little variation in cervical length was observed (7.2 and 5.5mm, respectively).
Patient 14 (figure 3, GA 24^{+1}), a high risk multiparous women on hydroxyprogesteron treatment, was examined 15 weeks prior to parturition. During the whole 30 minutes observation period peristaltic movement of the bowel was observed. This was associated with a transient shortening and curving of the cervical canal, which resulted in a shorter CL. However, only some of these peristaltic movements of the bowel appeared to alter the cervical shape.
Overall, peristaltic movement of the bowel appeared to be associated with fluctuations in the length of the cervical canal in 7 patients (patient 4;5;8;11;14;15;17). The amount of peristaltic movements (quantificated by the number of arrows in figure 4) was significantly correlated to the CL variation (Figure 5, Pearson correlation 0.80; P<0.01; 95% CI 0.54;0.92). However, it should be noted that much of this correlation is due to the two cases with a very high incidence of peristalsis.

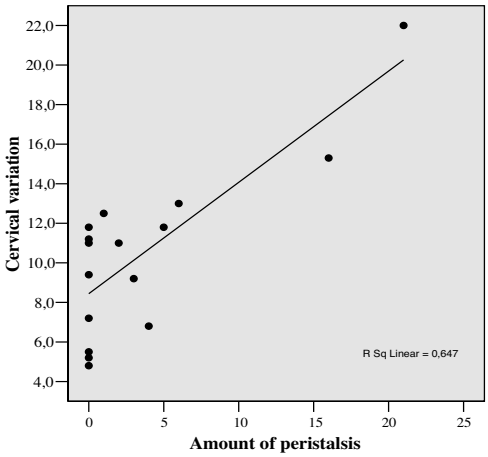

Figure 5: Correlation of the amount of peristalsis (quantificated by the number of arrows in figure 4), and variation in CL.

Fetal movements were observed in all patients. In 9 patients (patient 2;4;7;8;10;11;13-15) these movements were at times directed right at the cervix and this appeared to alter the shape of the cervical canal. In the other patients the cervix was not influenced by fetal movements.
No contractions were reported by the patients during the 30 minutes recordings. However, tocography showed 8 contractions in 3 patients, of which 2 were associated with shortening of the cervix.
In 5 patients (patient 1;3;9;16;18) without fetal movements directed at the cervix, and without peristaltic movement of the bowel or contractions, CL variation was smaller than in patients with one ore more of these conditions present (mean 6.1mm; range 1.6-9.4mm and mean 12.7mm; range 5.2-26.7mm, respectively). The difference in CL variation between women with these conditions present and absent was significant (P=0.03; mean difference 6.6mm; 95% CI 0.6;12.6mm).

Discussion

In this study, we performed continuous 30 minutes recordings of the cervix in the 2nd and 3rd trimester of pregnancy. We found a considerable variation in CL with time (mean 10.9mm). Variation was more pronounced in the presence of fetal movements directed towards the cervix, peristalsis or contractions. It was present both in nulliparous and parous women, and both in high and low risk women.
When standardized, the intraobserver difference of the CL measurement has been reported smaller than 5.0mm[10;11]. Furthermore, the interobserver difference in CL on fixed images has been found to be less than when real-time measurements were performed, suggesting true changes in CL during the examination[10].
Dynamic changes of the cervix have been reported by previous studies[8;9;12-15], and alterations in cervical appearance have been observed in nulliparous and parous women, in women who delivered preterm and at term. In most of these studies the cervix was observed less than 10 minutes. Some authors have observed dynamic changes more frequent in women with symptoms of threatened preterm labour[14;15]. In two patients who delivered preterm, the dynamic changes were observed 3 and 5 weeks before delivery[15]. To our best knowledge, these are the first observations of variation in CL during a 30 minutes period and associated with fetal movement or peristalsis.
In this study, we found a considerable variation in CL measurements during a continuous 30 minutes observation of the cervix. This variation was not related to GA or to ultrasound-delivery interval. It must be noted, however, that the number of patients in this study was small, and the range of GA at the time of the 30 minutes observation was large. Therefore, the prevalence and range of CL variation can not be determined from these findings.

In general, the CL cut-off point for the prediction of preterm delivery is considered to be between 15 and 25mm[16-19]. CL variation is only of clinical relevance, when the CL measurement varies around the cut-off point for threatened preterm delivery. Two patients (patient 2 and 18) had a cervix varying from <20mm to >20mm. The 30 minutes examinations were performed at 30^{+1} and 30^{+4} weeks of gestation, respectively, and the patients delivered 8 and 6 weeks later, respectively

In conclusion, we demonstrate that dynamic changes in CL are present at early gestation and long before delivery. Alterations in the appearance of the cervix can be observed either spontaneously or associated with contractions, fetal movements or peristalsis, and these conditions must be considered as pitfalls in CL measurement. In critical cases, such as early threatened preterm labour, increase of the frequency and duration of sonographic ultrasound measurements may be helpful to obtain a more reliable estimation of the cervical status. However, further research is necessary to investigate the predictive value of dynamic changes in CL for spontaneous onset of labour.

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4

Transperineal versus transvaginal sonographic cervical length measurement in preterm and term pregnancy

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Philip Stoutenbeek
Gerard H.A. Visser

Abstract

Objective The aim of this study was to investigate the reliability of and patient satisfaction with transperineal cervical length (CL) measurements during the third trimester of pregnancy and to compare this with measurements obtained during midtrimester.

Methods Women attending the outpatient clinic for a CL measurement before 29 weeks of gestation or after 35 weeks were examined by transvaginal and transperineal ultrasound. Preference for either method was indicated both by sonographers and patients.

Results Seventy one patients participated in the study, 23 preterm and 48 in the third trimester of pregnancy. There was 30% failure to obtain a clear image on transperineal ultrasound during the preterm period, and 19% in the third trimester. Elevation of the hips improved the image in 50% of these cases. Transvaginal CL measurements could be obtained in all cases. There was a strong correlation between transvaginal and transperineal measured CL (Pearson correlation 0.85). Sonographers preferred transvaginal images of the cervix both preterm and at the third trimester. Transperineal ultrasound was valued not or mildly painful by most women, however transvaginal ultrasound was appreciated best.

Conclusions The findings of this study demonstrate that transvaginal ultrasound is the least painful, most feasible, and probably the most accurate method to measure CL in the third trimester of pregnancy. Transperineal ultrasound can be a feasible alternative for transvaginal ultrasound, however its application in clinical practice is restricted by the need for an experienced sonographer.

Introduction

Sonographic cervical length (CL) measurements are used to predict the timing and course of labour, both at midgestation and in the term period. The gold standard for cervical assessment is transvaginal ultrasound[1]. Two other approaches have been reported previously, namely transabdominal and transperineal ultrasound. Transabdominal imaging of the cervix is limited by the position of the fetal head, especially with advanced gestational age. Moreover, in case of a short cervix it is difficult to obtain a clear image[2]. Visualization of the cervix is improved by bladder filling, but this is known to artificially elongate the cervical canal[2-4]. With transperineal sonography of the cervix one does not encounter these difficulties.

The reliability of transperineal CL measurements has mainly been investigated in very preterm pregnancies, with two studies including gestational ages of 30-34 weeks, and one study which also included term gestations, but without distinction being made between preterm and term[5-11]. The transperineal method correlates well with the transvaginal method and is considered to be dependent on experience of the investigator. Failure to obtain a clear image has been reported in 0-12% of the cases, and is mainly due to shadowing by bowel gas or the pubic symphysis. In such cases, elevation of the hips may improve the image of the cervix.

It has been reported that transperineal ultrasound may be helpful to predict the course of labour in women with prelabour rupture of the membranes (PROM) at term[12]. However, the reliability of this method compared to transvaginal ultrasound has not well been demonstrated beyond 34 weeks of gestation. Although transvaginal ultrasound does not seem to increase perinatal infection[13], and the method is being used in case of preterm PROM[14], investigating the feasibility of the transperineal method at term is of interest for clinicians who are reluctant to use transvaginal ultrasound in case of PROM.

The aim of this study was to investigate feasibility and reliability of transperineal CL measurements in the third trimester of pregnancy and to compare this with CL measurements in the preterm period to be able to relate our results to previous literature. Furthermore, patient satisfaction with the transperineal method was measured by a painscore and compared to transvaginal ultrasound and digital examination of the cervix. This gives information about the acceptability of the transperineal method at term for both clinicians and patients and this has only been investigated in one earlier study[6].

Materials and Methods

Low risk women, who would not have otherwise had a CL measurement, with singleton pregnancies beyond 35 weeks of gestation and a fetus in cephalic position (third trimester

group), and high risk women who attended the outpatient clinic for a transvaginal CL measurement before 29 weeks of gestation (preterm group) were asked to participate in the study. All women gave informed consent before the start of the ultrasound examination. The transvaginal CL measurements were performed with a 6-MHz endovaginal transducer (APLIO, Toshiba Medical Systems, Tokyo). Women were asked to empty the bladder. Care was taken to avoid pressure on the cervix and the CL was determined in a sagittal plane of the cervix with a clear image of the internal and external os and the complete cervical canal. The transperineal CL measurements were performed with a 3.5-MHz transducer (APLIO, Toshiba Medical Systems, Tokyo). The transducer was rotated until a clear image of the complete cervical canal and internal and external os was obtained. Women were in the supine position. When multiple CL measurements were obtained, the shortest best CL was used for analysis. All transvaginal measurements were obtained by a single sonographer (M.M.) and all transperineal measurements were obtained by another sonographer (Ph.S.), who had 30 years experience with sonography. Both sonographers were blinded for the CL measurements of the other. Alternately, the transvaginal and transperineal CL measurement was taken first, and a maximum of 15 minutes was aimed for between the transvaginal and transperineal examination. Figure 1 shows examples of transvaginal and transperineal images of the cervix.

When the study was completed, all transvaginal and transperineal images were analyzed separately by the sonographers to assess reliability. When one of the three landmarks of the cervix -the internal and external os and the cervical canal- was in retrospect unclear, the image was considered a failure and was excluded from analysis. Each sonographer indicated by which method the landmarks were most certain and by which the most accurate CL measurement could be obtained. A third experienced sonographer (L.P.) was asked to qualify the images by scoring the three landmarks of the cervix as either clear (2), uncertain (1) or not visible (0). The total score (0-6) for each method was compared.

After delivery, the women who participated in the study in the third trimester of pregnancy were asked to indicate on a 1 to 5 scale (1 = not painful; 5 = extremely painful) the painfulness of transvaginal US, transperineal US, and digital examination of the cervix either antenatally, or during early labour.

Statistical analysis was performed with the SPSS 12.0 statistical package. A paired t-test and Pearson correlation were used to determine the agreement between transvaginal and transperineal measured CL. The independent-samples t-test was used to detect differences in CL between the third trimester and preterm group. To detect a difference larger than 5mm between the transvaginal and transperineal measured CL with a Power of 0.90, the calculated sample size was 23. Qualification of the transvaginal and transperineal images by scoring the landmarks (0-6) was analyzed by the Wilcoxon signed ranks test. The painscore of the three examination methods were analyzed by the non-parametric Friedman test and Wilcoxon signed ranks test. P values <0.05 were considered statistically significant.

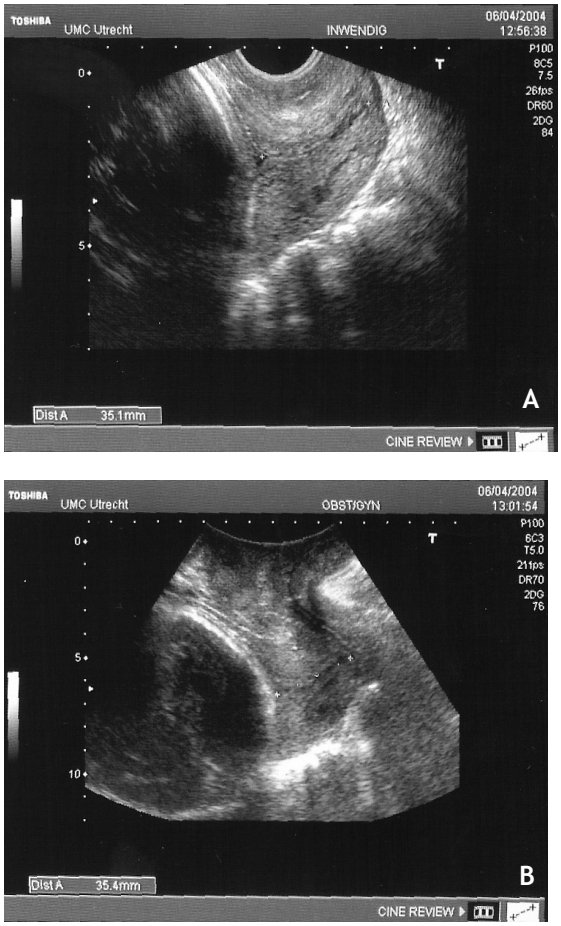

Figure 1: Transvaginal (A) and transperineal (B) images of the cervix.

Results

Seventy one women participated in the study. The third trimester group consisted of 39 nulliparous women and 9 women with a previous caesarean section. Mean gestational age (GA) at ultrasound examination was 38 weeks (range 35-41 weeks). The preterm group consisted of 23 women with a previous preterm delivery. Mean GA in this group was 20 weeks (range 11-28 weeks). Most women were Caucasian (94%) and 6% Asian. The median maternal age was 33 years (range 20-47 years).

In the third trimester group, the mean transvaginal CL measurement was 34mm (range 18-52mm). In two cases, images were not documented and could therefore not be assessed for their reliability. In 9 out of 48 cases (19%) it was not possible to obtain a clear image of the internal os, external os and cervical canal by transperineal sonography, due to shadowing.

In the preterm group, the mean transvaginal CL was 42mm (range 26-74mm). In this group, we failed to obtain a clear image of the cervix by transperineal sonography in 7 out of 23 cases (30%). In 10 cases in which no clear image could be obtained we repeated the observation after elevation of the hips and obtained an adequate image in 5 of them (50%). All transvaginal images were assessed as being reliable.

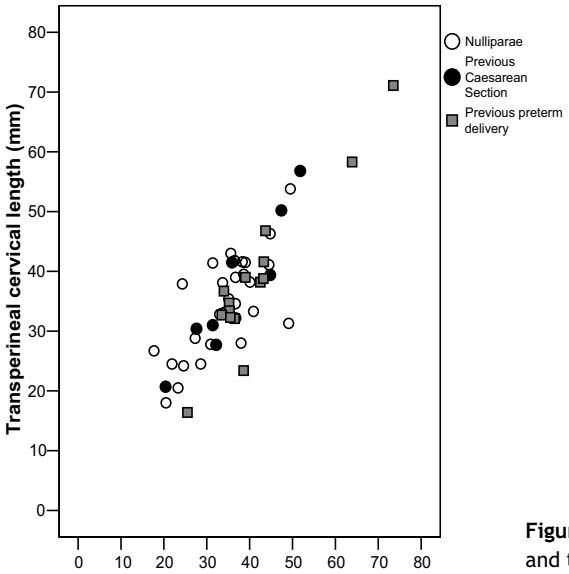

Figure 2: Correlation between transvaginal and transperineal measured CL.

Figure 2 depicts the association between the transvaginal and transperineal measured CL. Overall, there was a strong correlation (n=54; Pearson correlation 0.85; P<0.01; 95% CI 0.75;0.91). There was a mean difference in CL, defined as transvaginal minus transperineal CL, of -0.3mm (SE 0.9mm) in the third trimester group, and of 3.2mm (SE 1.2mm) in the preterm group (Figure 3: Bland Altman plot). The correlation between the two methods was stronger preterm (Pearson correlation 0.94; P<0.01; 95% CI 0.82;0.98) than during the third trimester (Pearson correlation 0.79; P<0.01; 95% CI 0.63;0.88). In 24% of cases, the difference in CL was more than 5mm, and in 5 out of 54 cases (10%) the difference was more than 10mm. In retrospect, from these 5 cases the cervical canal was assessed erroneously once using transvaginal ultrasound, and once with transperineal ultrasound. In another case the cervix was observed from a different angle at transperineal and transvaginal ultrasound. In the other two cases the difference remained unexplained. The difference between transperineal and transvaginal measured CL was not correlated with the time interval between the two methods (Pearson correlation 0.01; P=0.95; 95% CI -0.26;0.28).

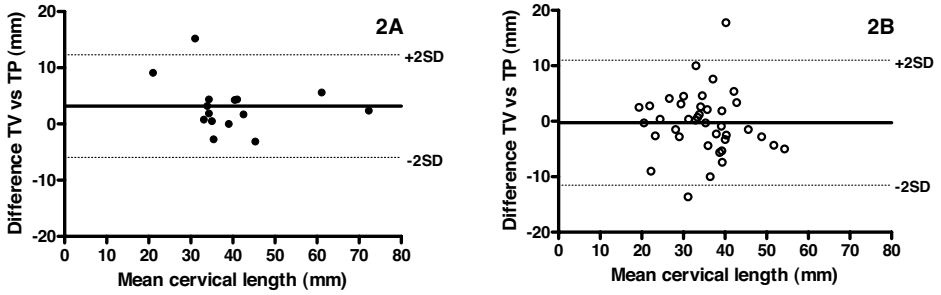

Figure 3: Bland-Altman plot of the difference between transvaginal and transperineal measured cervical length versus the mean cervical length at midtrimester (2A) and third trimester (2B).

The accuracy of identification of a short cervix -less than 25mm- by transperineal ultrasound was determined, using the transvaginal measurement as the gold standard (Table I). There was a significant association between a short cervix on transvaginal and transperineal ultrasound (Fisher's Exact Test P<0.01). In case of a short cervix on transvaginal ultrasound, transperineal sonography was moderately accurate: sensitivity 71%; specificity 94%; positive predictive value 63%; and negative predictive value 96%.

Both sonographers (M.M. and Ph.S.) were asked by reviewing the images to indicate which of the two methods provided the most accurate view of the cervical canal. In the third trimester of pregnancy, the transvaginal approach was preferred in half of the cases by both sonographers (47% and 53%, respectively - Figure 4). However, the transperineal approach provided equally accurate images in 32% to 49% of cases, and better images in a minority of the cases (4% and 15%). In the preterm period, most transvaginal images were preferred to the transperineal images (78% and 91%, respectively). Both sonographers indicated that a cephalic position of the fetus was helpful for accurately estimation of the three landmarks -the internal and external os and the cervical canal- on transperineal ultrasound. The third sonographer valued the three landmarks of the cervix significantly better visible at transvaginal ultrasound than at transperineal ultrasound, irrespective of the trimester in which the images were performed (Wilcoxon signed rank test P<0.01; median score 6, range 3-6 and median score 5, range 0-6 respectively).

In the third trimester women appreciated transvaginal ultrasound best (94% not or mildly painful – Figure 5). Mean painscore for transvaginal sonography was 1.5 (range 1-3) compared to 2.0 (range 1-5) for transperineal sonography and 3.0 (range 1-5) for digital examination of the cervix. Transperineal ultrasound was valued not or only mildly painful in 68% of the cases, and although valued more painful than transvaginal ultrasound (Wilcoxon signed rank test; P=0.01), it was significantly less painful than digital examination of the cervix (Wilcoxon signed ranks test; P<0.01).

Table I: Accuracy of detection of a short cervix on transperineal ultrasound

	Transperineal < 25mm	*Transperineal > 25mm*	*Total*
Transvaginal < 25mm	5	2	7
Transvaginal > 25mm	3	44	47
Total	8	46	54

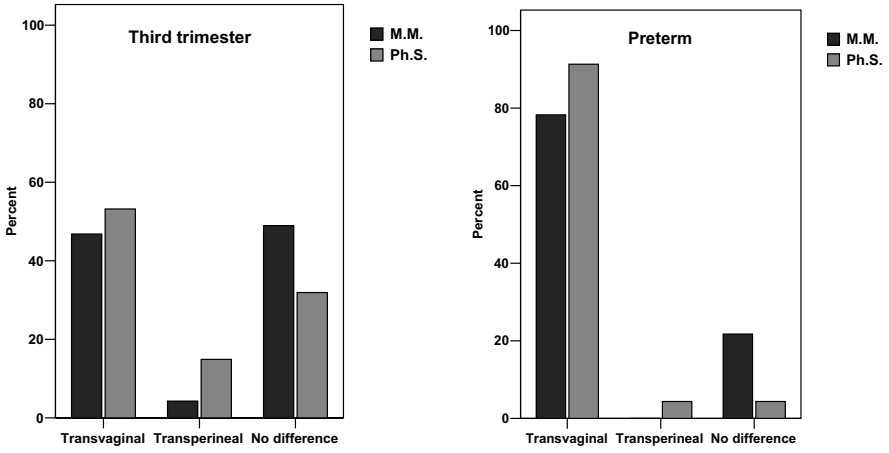

Figure 4: Preference for the different methods of CL measurements by the two sonographers (M.M. and Ph.S.)

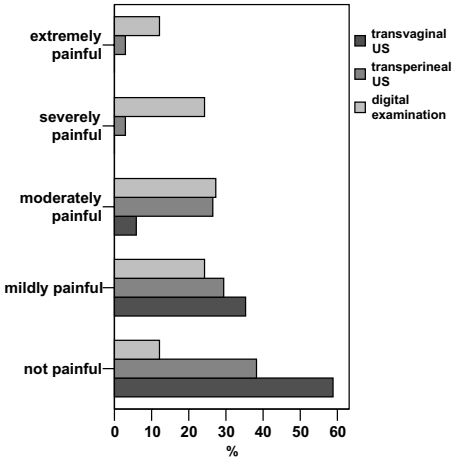

Figure 5: Painscore for the different methods of examining the cervix, indicated by women in the third trimester group.

Discussion

The findings of this study demonstrate that transvaginal ultrasound is the least painful, most feasible, and probably the most accurate method to measure CL in the third trimester of pregnancy. However, the transperineal method appears to be a reasonable alternative in cases when transvaginal ultrasound is undesirable. It may be offered to women who object against transvaginal ultrasound and may be used in case of ruptured membranes and expectant management, although transvaginal ultrasound does not seem to increase the risk of perinatal infection (at least not in one study including 92 patients)[13].

A limitation of this study was the limited experience of our sonographers with transperineal ultrasound of the cervix. This resulted in relatively high percentage of failure of obtaining a clear image of the cervix on transperineal ultrasound as compared to the 7 previous studies[5-11] (Table II). Accurate estimation of the three landmarks at transperineal ultrasound was especially difficult in case of shadowing of bowel gases and a non-cephalic position of the fetus, and this was more definite in the preterm period. Furthermore, elevation of the hips improved the image more frequent in the third trimester than in the preterm period of pregnancy. This suggests that obtaining a clear image of the cervix by transperineal ultrasound is easier in the third trimester of pregnancy than in the preterm period.

Table II: Transvaginal (TV) versus transperineal (TP) CL

Study characteristics

Author	*Nr*	*GA*	*Object*	*Position*	*Experience*	*Failure*	*Mean diff (range mm)*	*Correlation*
Berghella et al. 1997	1110	18-25	Funneling	Supine		0%		0.82
Kurtzman et al. 1998	206	14-34	CL Funneling	Elevated hips or stirrups	100 TP scans	0%	1 (-5.7;4)	0.95
Owen et al. 1999	102	15-24	CL Funneling	Supine	>10 years TV	11%	1.6 (-19;27)	0.38
Carr et al. 2000	84	14-40	CL	Supine	3 years TP	5%	5 (1;23)	0.77
Cicero et al. 2001	300	22-24	CL	Supine	>2000 TV / 65 TP scans	12%	0.2 (-5.8;6.1)	0.93
Yazici et al. 2004	357	24	CL	Elevated hips		11%		0.83
Ozdemir et al. 2005	36 32 33	10-14 20-24 30-34	CL Funneling	Elevated hips		3% 0% 0%	2.8 ± 2.3 0.9 ± 1.3 0.5 ± 1.4	0.93 0.97 0.97
Meijer et al. (Present study)	*23* *48*	*11-28* *35-41*	*CL*	*Supine*	*30 years TV*	*30%* *19%*	*3.2 ± 2.4* *-0.3 ± 1.8*	*0.94* *0.79*

Overall, there was a good correlation between transvaginal and transperineal measured CL. However, in the preterm group there was a larger difference between the two methods with a stronger correlation than in the third trimester group, suggesting a systematic error in either the transperineal or the transvaginal measurements in the preterm period. This is in agreement with a previous study in which a difference larger than 5mm in 10% of all cases was found, with CL being larger at transvaginal ultrasound[6]. Pressure on the transvaginal transducer is known to artificially elongate the cervical canal[15] and this may account for the difference in CL between the two methods. The preterm group consisted only of multiparous women, and the third trimester group of nulliparous women and women with a previous caesarean section, who may be considered nulliparous women. Therefore, parity may account for the larger difference between the two methods in the preterm group than in the third trimester group.

Previous studies have demonstrated that transperineal measured CL correlates well with transvaginal measured CL[5-8;10;11]. When sonographers are experienced and when women are placed in the elevated hip position, a correlation of 0.95 and failure of 0% has been reported[8]. Cicero et al[7] demonstrated at midgestation that failure to obtain a clear image of the cervix at transperineal ultrasound decreased from 55% to 12% after an initial learning period. Furthermore, Ozdemir et al[10] investigated the reliability of transperineal ultrasound in three groups: 10-14 weeks GA, 20-24 weeks GA and 30-34 weeks GA. As pregnancy progressed, the correlation between transvaginal and transperineal measured CL became stronger, and the difference between the two methods smaller. In our study, the percentage of failure was also smaller in the third trimester than in the preterm period.

Less outstanding were the results of a study performed by Owen et al[9]. This study was performed at early gestation (52 out of 102 cases before 20 weeks GA), there was limited experience with transperineal sonography and the elevated hip position was not used. In 50% of the cases, a difference of more than 10% was found between the transvaginal and transperineal measured CL, this difference was even more than 20% in one third of the cases. This emphasizes the need for an experienced sonographer when transperineal CL measurements are performed.

In a previous study[7], patients tolerated transperineal ultrasound of the cervix better than transvaginal ultrasound. Our patients valued transperineal ultrasound in the third trimester more painful than transvaginal ultrasound, although it was significantly less painful than digital examination of the cervix. This might be due to the fact that the sonographers in the quoted study were more experienced with transperineal ultrasound, which might result in less pressure on the ultrasound probe during the transperineal investigation. Furthermore, it must be noted that digital examination of the cervix was sometimes performed during labour, which may explain the difference in patient tolerance with prelabour ultrasound examination. In the present study, sonographers were more satisfied with the transvaginal images of the cervix, particularly in the preterm period. In the third trimester, the satisfaction did not differ largely.

The results of our study suggest that transperineal ultrasound can be a feasible alternative for transvaginal ultrasound of the cervix. With advanced gestation, the success of obtaining a clear image of the cervix by transperineal ultrasound appears to improve. However, we support the suggestion that the accuracy of transperineal sonography is dependent on the experience of the sonographer with this specific method, which restricts its application in clinical practice.

Acknowledgement

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5

Sonographic longitudinal cervical length measurements in nulliparous women at term; prediction of spontaneous onset of labour

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Abstract

Introduction The aim of this study was to predict spontaneous onset of labour by serial transvaginal ultrasound in a homogenous population of nulliparous women at term.

Methods One hundred sixty two nulliparous women with a singleton fetus in cephalic position were examined at weekly intervals from 36 weeks of gestation to delivery. Cervical length (CL) was measured by transvaginal ultrasound in supine and upright position.

Results There was a significant decrease in CL in the last twelve days prior to delivery, however this decrease was small with a substantial variation between individuals. Women with a spontaneous onset of labour could be divided into three different groups: unchanged CL until shortly before delivery, a drop in CL in the last two weeks prior to delivery, and a gradual change in CL starting before the last two weeks prior to delivery. A single CL measurement smaller than 30mm in supine and upright position between 37 and 38 weeks of gestation was predictive for spontaneous onset of labour before 41 weeks of gestation (sensitivity 46%; specificity 78%; PPV 82%; NPV 40% and sensitivity 53%; specificity 72%; PPV 81%; NPV 40% respectively).

Conclusion Between 37 and 38 weeks of gestation, spontaneous onset of labour before 41 weeks of gestation can be predicted by a CL measurement, but with low sensitivity and NPV. Inter-individual variation in CL and in CL changes is large. This hampers the predictive value of single and repeated CL measurements for the spontaneous onset of labour.

Introduction

Sonographic cervical length (CL) measurements have been used to predict preterm birth. In women with symptoms of preterm labour, a CL less than 15mm is predictive for delivery within 7 days[1;2]. However, in a general population at midtrimester, the negative predictive value (NPV) of CL measurements is high and the positive predictive value (PPV) low. In a general population, midtrimester screening is therefore only helpful to identify patients at low risk for preterm delivery[3].
According to both Rozenberg et al[4] and Bayramoglu et al[5] the PPV of a single CL measurement in the term period of pregnancy is high and as good as digital examination of the cervix in predicting spontaneous onset of labour within 7 days[4]. Such a prediction might be helpful in the decision-making process for induction of labour or otherwise. Data on the term period are, however, scarce[6-9] and data from serial CL measurements at term are lacking apart from two small studies[6;7].
The aim of this study was to observe cervical changes by serial transvaginal ultrasound, both in supine and upright position, preceding spontaneous onset of labour in a homogenous population of nulliparous women at term. We hypothesized that the onset of labour might be predicted by sonographic CL and/or changes in CL. Understanding the normal evolution of the CL at term might be helpful in cases in which induction of labour is considered.

Materials and methods

Nulliparous women with a singleton fetus in cephalic position were recruited at the University Medical Center, Utrecht, The Netherlands, and at the Hospital Oost-Limburg, Genk, Belgium, between February 2004 and June 2006. Exclusion criteria were admission for threatened preterm labour earlier in pregnancy and previous exconisation of the cervix. Sonographic CL measurements were taken at weekly intervals from 36 weeks of gestation onwards. Women were asked to empty the bladder before the examination. First, the amnion fluid index (AFI) was determined by abdominal ultrasound (3.5-MHz transducer; APLIO, Toshiba Medical Systems, Tokyo; Esaote Technos, Genova, Italy) as previously described[10]. Thereafter, the CL was measured by transvaginal ultrasound (6-MHz endovaginal transducer, APLIO, Toshiba Medical Systems, Tokyo; 7.5-MHz endovaginal transducer- Esaote Aquila, Genova, Italy). Subsequently, the CL was measured with the woman in the upright position for at least 1 minute. The transvaginal ultrasound probe was withdrawn until a sagittal view of the cervix was obtained without distortion of the shape by pressure of the ultrasound probe. CL was measured from the internal to the external os, with a clear view of the cervical canal. Funneling was considered present when funnel length, measured from the internal os to the fetal occiput, was more than 5mm.

Statistical analysis was performed with SPSS 12.0. The Pearson correlation coefficient was used to quantify the association between CL measurements in the supine and upright position, and the association between CL and AFI at gestational age (GA) at ultrasound and ultrasound-delivery interval, respectively. The difference of supine minus upright measured CL was depicted versus the mean CL in a Bland-Altman plot. The ANOVA for repeated measurements was used to quantify the within subjects difference for CL measurements in supine and upright position in the last three weeks before spontaneous onset of labour. A Cox regression analysis was performed to evaluate the effect of CL measurements between 37 and 38 weeks of gestation on the number of days until delivery. P values <0.05 were considered statistically significant.
The study was approved by the local Medical Ethics Committee and all women gave written informed consent.

Results

A total of 162 nulliparous women participated in the study. Mean maternal age was 31 years (range 20-42). Most women were Caucasian (97%) and 3% Asian. Mean GA at delivery was 281 days (range 258-298 days). Spontaneous onset of labour occurred in 123 women (76%); in 39 women (24%) labour was induced for medical indications, in 25 women before 41 weeks of gestation and in 14 women beyond 41 weeks of gestation. Of the women with a spontaneous onset of labour, 85% delivered vaginally, 11% had a caesarean section (CS) for failure of progress and 4% had an emergency CS. In the induction group, 74% delivered vaginally, 13% had a CS for failure of progress and 13% had an emergency CS.
The difference in CL measured in the supine and upright position was determined in the last three weeks before spontaneous onset of labour. Only women with spontaneous onset of labour and at least three subsequent ultrasound examinations were included in this analysis (n=60). CL in supine position was strongly correlated with CL in upright position in the last week before spontaneous onset of labour (Figure 1, mean difference 1.9mm; 95% CI 0.8;3.2mm; Pearson correlation 0.90; P<0.01; 95% CI 0.84;0.94), and this correlation did not change in the three weeks preceding the spontaneous onset of labour (1-2 weeks before delivery Pearson correlation 0.90; P<0.01; 95% CI 0.84;0.94 and 2-3 weeks before delivery Pearson correlation 0.88; P<0.01; 95% CI 0.81;0.93).

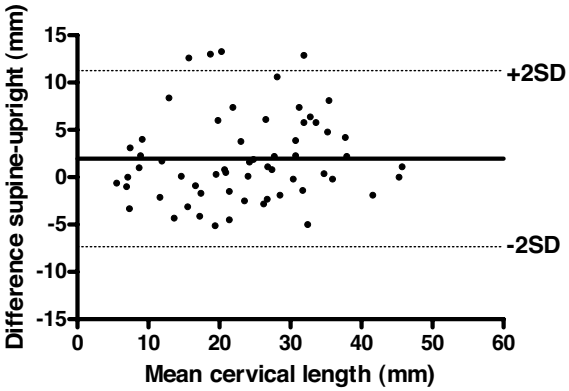

Figure 1: Bland-Altman plot of the difference between the last CL measurement in supine and upright position.

The last CL measurement in supine position of all 123 women with a spontaneous onset of labour was used to determine the correlation with GA at ultrasound examination and ultrasound-delivery interval (Figure 2). The mean ultrasound-delivery interval was 4 days (range 0-12 days) and in 44 cases (36%), the ultrasound was performed within 48 hours to delivery. CL measurements correlated significantly with the ultrasound-delivery interval (Pearson correlation -0.26; P=0.01; 95% CI -0.45;-0.05), but not with GA at ultrasound examination (Pearson correlation -0.05; P=0.64). Also, the last AFI measurement in these women correlated significantly with the ultrasound-delivery interval (Pearson correlation -0.22; P=0.02; 95% CI -0.38;-0.04), but not with the GA at ultrasound examination (Pearson correlation -0.08; P=0.36 – Figure 3). However, the decrease in both CL and AFI in the last twelve days prior to delivery was small with a substantial variation. Furthermore, in 31% of the women the last CL measurement before spontaneous onset of labour was greater than 30mm, and in 24% when the last CL was taken within 48 hours to delivery.

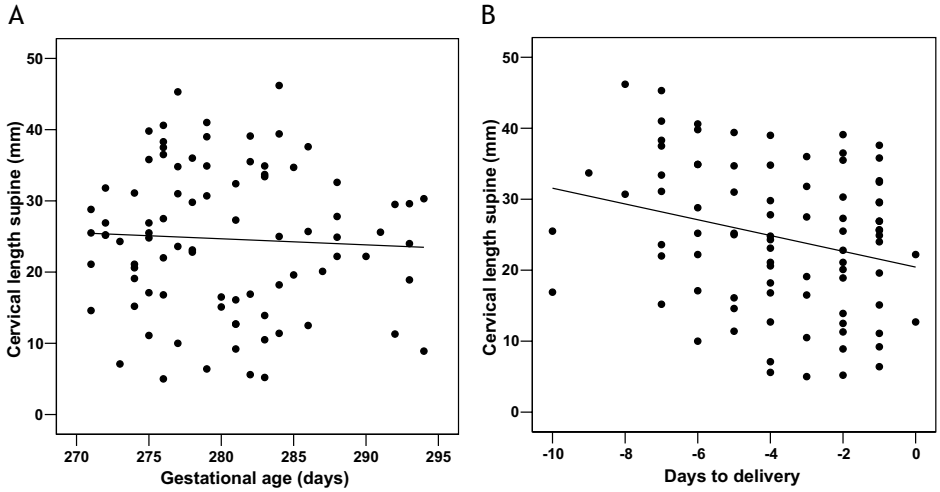

Figure 2: Correlation between the last CL measurement and GA (figure 2A) and days to delivery (figure 2B).

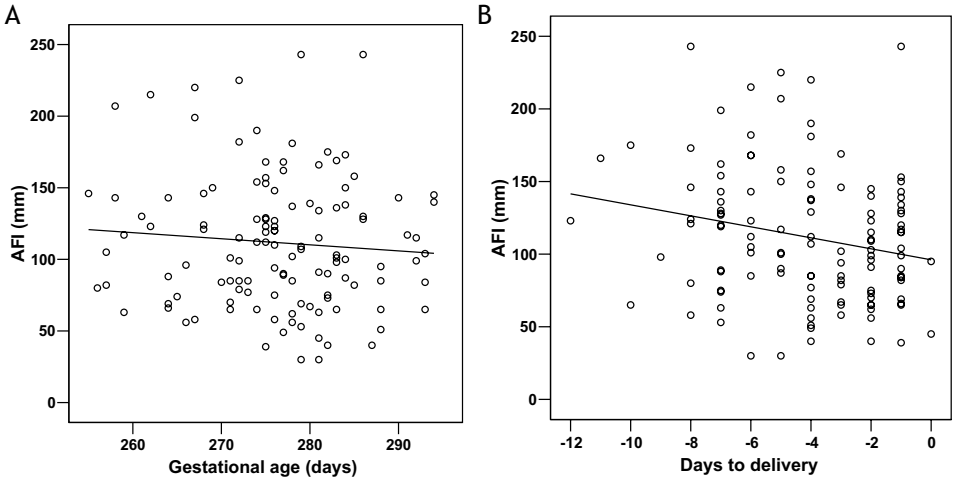

Figure 3: Correlation between the last Amnion Fluid Index (AFI) and GA (figure 3A) and days to delivery (figure 3B).

When individual plots of the change in CL over the observation period were made, we observed different patterns between women (Figure 4). Women with a spontaneous onset of labour, a minimum of three ultrasound observations and a last measurement within 7 days to delivery, could be divided into three different groups. Women were classified as group A (n=48) when CL did not change prior to delivery (defined as a decrease in CL less than 5mm per week). Women with a decrease in CL of at least 5mm per week were classified as either group B (n=19) or C (n=21) according to the occurrence of this decrease, within or already before the last two weeks prior to delivery, respectively.

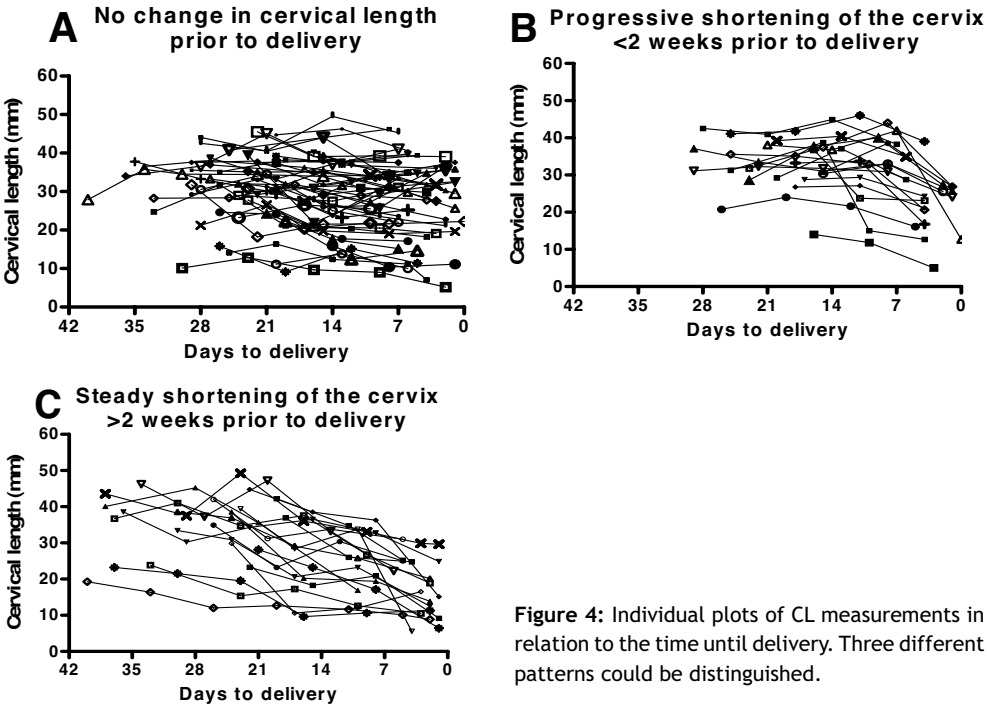

Figure 4: Individual plots of CL measurements in relation to the time until delivery. Three different patterns could be distinguished.

Since inter-individual variation was large throughout the term period, we used only the CL between 37 and 38 weeks of gestation to predict spontaneous onset of labour. For this analysis, we included all women who had spontaneous onset of labour before 41 weeks of gestation (n=93), and women who delivered beyond 41 weeks of gestation, irrespective of the onset of labour -spontaneous (n=30) or induced (n=14)-. Twenty out of these 137 women had to be excluded since the first CL was measured between 38 and 39 weeks of gestation. In another 13 women the upright CL measurement was missing. There was a decrease in hazard ratio of 32% and 29% respectively, for spontaneous onset of labour with every 10mm increase in supine and upright CL (HR=0.68; 95% CI 0.55;0.85 and HR=0.71; 95% CI 0.58;0.88, respectively). Survival analysis indicated that cumulative probability of remaining undelivered with time was significantly different in women with a CL of 31-40mm or 41-50mm at 37 weeks of gestation, than in women with a CL smaller than 20mm (HR=0.44; P<0.01; 95% CI 0.26;0.75; and HR=0.36; P<0.01; 95% CI 0.17;0.73). There was no significant difference between the group with a CL smaller than 20mm and 21-30mm (HR=0.68; P=0.19; 95% CI 0.39;1.21). Data for CL measurements in upright position were similar (not shown). Table 1 shows a 2x2 contingency table for supine and upright CL measurement at 37 weeks of gestation. A CL less than 30mm was predictive for spontaneous onset of labour before 41 weeks of gestation (supine: sensitivity 46%; specificity 78%; PPV 82%; NPV 40% and upright: sensitivity 53%; specificity 72%; PPV 81%; NPV 40%).

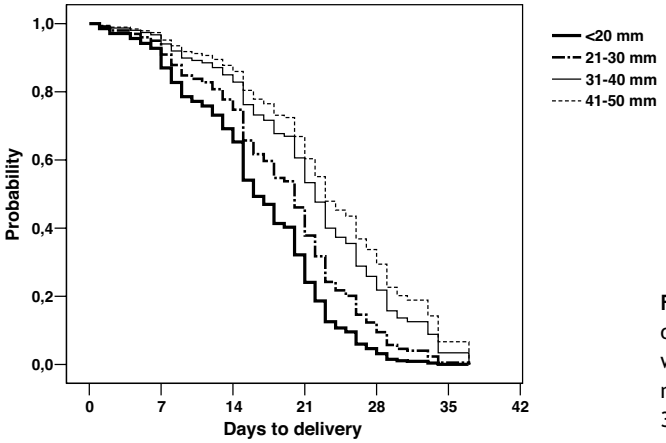

Figure 5: Cumulative probability of remaining undelivered at 41 weeks of gestation for a single CL measurement in supine position at 37 weeks of gestation.

Table 1: 2 x 2 contingency table for the prediction of spontaneous onset of labour before 41 weeks of gestation by a CL measurement in supine (1A) and upright position (1B) at 37 weeks of gestation.

1A	Spontaneous onset of labour before 41 weeks of gestation		Total
	Yes	No	
CL supine < 30 mm	37	8	45
CL supine ≥ 30 mm	43	29	72
Total	80	37	117

1B	Spontaneous onset of labour before 41 weeks of gestation		Total
	Yes	No	
CL upright < 30 mm	38	9	47
CL upright ≥ 30 mm	34	23	57
Total	72	32	104

Discussion

We demonstrated a large inter-individual variation in CL and in CL changes before the spontaneous onset of labour at term. The last CL measurement was only weakly correlated with the time until spontaneous onset of labour, and even in the last 48 hours prior to delivery, a quarter of our population still had a CL greater than 30mm. CL was not correlated with gestational age. The findings of CL and AFI in relation to gestational age and onset of labour were identical and the AFI data were in accordance with earlier data[10]. In only half of the population we found a decrease in CL preceding labour, either gradual over the weeks or within the last two weeks before delivery. In the others CL remained unchanged until shortly before delivery. This large variation interferes with the prediction of spontaneous onset of labour by a single CL measurement at any point in time at term.

Previous studies have reported normal ranges for CL during pregnancy[8;9;11;12], but this is the first study in which individual patterns in CL in a large and homogenous population of nulliparous women were investigated longitudinally. Bergelin et al performed CL measurements every two weeks from midgestation to delivery at term in 19 nulliparous women[6], and 21 parous women[7]. In most women they found a gradual or accelerated decrease in CL prior to delivery. Our data indicate that in about half of the nulliparous population no CL changes occur in the 3 to 5 weeks prior to delivery, at least not until 48 hours before spontaneous onset of labour.

Two earlier studies investigated the sonographic CL at 37 weeks of gestation as a predictor of spontaneous onset of labour before 41 weeks of gestation[5;13]. They found a high PPV (95% and 92%, respectively) with a CL of 30mm as an optimal cut-off point. Our data confirm the latter finding, but sensitivity and NPV were low. These findings were similar for CL measurements taken in supine and upright position.

In conclusion, inter-individual variation in CL and in CL changes are large at term. This large variation interferes with the prediction of spontaneous onset of labour by a single CL measurement at any point in time. Only a CL <30mm between 37 and 38 weeks of gestation appears to predict spontaneous onset of labour before 41 weeks of gestation, but with low sensitivity and NPV.

Acknowledgement

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6

Prediction of the outcome of labour induction at term by transvaginal ultrasound in supine and upright position

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Gerard H.A. Visser

Abstract

Introduction Aim of this study was to examine the predictive value of cervical length (CL) as measured by transvaginal sonography (TVS) in supine and upright maternal position on the outcome of induction of labour at term, and to compare these measures with the Bishop Score.

Methods TVS and digital examination of the cervix was performed in 73 nulliparous and 34 parous women before induction of labour at term. The Bishop Score and TVS parameters were used for the prediction of a vaginal delivery after labour induction.

Results Logistic regression analysis showed that only the CL in upright position was a significant predictor of the risk of caesarean section (CS) (OR 1.14; 95% CI 1.02;1.27). The area under the curve for the risk of a CS due to failure of progress was higher for the CL, either in supine or upright position, than for the Bishop Score (0.66, 0.68 and 0.46 respectively). Only the Bishop Score correlated significantly with the induction-to-delivery interval. However, when oxytocin and prostaglandin induction were analyzed separately, the latter correlation was not significant anymore.

Conclusion Sonographic CL measurements, especially in upright position, are better indication of the risk of CS after induction of labour than the Bishop Score. The latter correlates better with the duration of labour.

Introduction

Approximately 15% of all pregnancies are induced for medical indications around term. Compared to spontaneous onset of labour, induction of labour is complicated by a higher caesarean section (CS) rate[1;2]. This holds especially for nulliparous women with an unfavourable cervix[3]. Nulliparity is also associated with a longer duration of induced labour[4] and this is probably due to a later occurrence of the acceleration phase than in parous women[5]. Traditionally, the Bishop Score is used to assess pre-induction cervical ripeness. In the last decade, pre-induction sonographic cervical length (CL) determined by transvaginal sonography (TVS) has been investigated as an alternative for digital assessment of the cervix, since it is considered to be reproducible[2;6;7], easy to learn[8] and with images that can be documented for intra- and inter-observer comparison. Initial changes at the internal os of the cervix can be observed by TVS, even in the absence of cervical dilatation. Data on the predictive value of CL measurements in the upright position on outcome of induction of labour are lacking. Funneling may be masked when the cervix is only examined in supine position[9;10]. In addition, it has been shown that the accuracy of risk assessment of preterm birth is improved by maternal postural change[10;11].
Aim of this study was to determine the predictive value of CL as measured by TVS in supine and upright maternal position on the outcome of induction of labour at term and to compare those data with that of the Bishop Score.

Materials and methods

Between February 2004 and September 2006, women attending the University Medical Center, Utrecht and the Isala Clinics, Zwolle, The Netherlands, for induction of labour at term were asked to participate. Exclusion criteria were multiple gestation, non-cephalic presentation, and previous exconisation. TVS was performed immediately before induction, with the women in supine position for at least 5 minutes and with an empty bladder. After insertion, the transvaginal probe was withdrawn to avoid pressure on the cervix. A sagittal plane of the cervix was obtained with a clear view of the complete cervical canal and CL was measured from the internal to the external os. The examination was repeated with the women in upright position, at least 1 minute after the postural change. The shortest, best visualized CL out of three measurements was used for analysis. The measurements were performed using a 6-MHz endovaginal transducer (APLIO, Toshiba Medical Systems, Tokyo) or 8.5-MHz endovaginal transducer (ATL 5000 HDI, Philips Eindhoven, The Netherlands). The difference in CL was defined as supine minus upright measured CL. Furthermore, this difference was expressed as percentage of the CL in a supine position. Funneling was defined as opening of the internal os with herniation of the fetal membranes (Figure 1A). The presence or absence of funneling was recorded as well as funnel width, measured at the

level of the former internal os, and funnel depth, measured from the cervical canal to the level of the former internal os. The latter was used to calculate funneling as a percentage of the residual CL. Dilatation of the cervical canal was defined as a parallel echolucent zone extending from the internal to the external cervical os (Figure 1B).

Before induction clinicians, who were blinded for the ultrasound results, determined a modified Bishop Score[14] by digital examination of the cervix, using a 10 point scale. Patients with less than 2cm dilatation received prostaglandin E2 (PGE2) intravaginally. In patients with a more favourable cervix oxytocin was administered intravenously after artificial rupture of the membranes. A vaginal delivery was considered as a successful induction. The induction-to-delivery interval was defined as the period (hours) from the first administration of PGE2 or oxytocin to delivery.

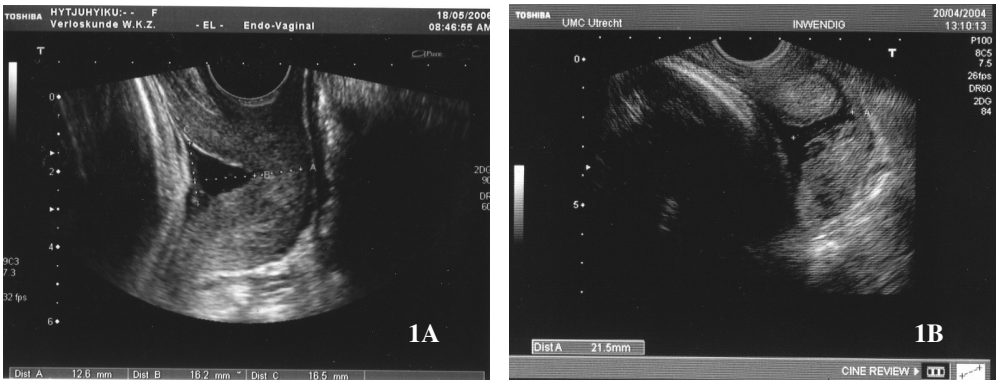

Figure 1: Examples of funneling (1A) and dilatation of the cervical canal (1B) on TVS of the cervix.

Statistical analysis was performed with SPSS 12.0. The Pearson correlation coefficient was used to quantify the association between the TVS parameters or digital examination and induction-to-delivery interval. A Bland-Altman plot was performed to depict the difference of supine minus upright measured CL versus the mean CL. A logistic regression analysis was used to quantify the odds ratio for the risk of a CS due to failure of progress. Women with a CS for fetal distress were excluded from this analysis. Fetal birthweight, gestational age at induction, PGE2 use, maternal age and maternal BMI were considered as confounding factors, and were used for a multivariable logistic regression analysis. ROC curves were performed to compare the likelihood of a CS for failure of progress between the CL in supine and upright position and the Bishop score. P values <0.05 were considered statistically significant.

The study was approved by the local Medical Ethics Committee, and all women gave written informed consent.

Results

A total of 107 women agreed to participate. Patient characteristics are shown in Table I. The most common indication for induction was post term pregnancy (45%).
The CL measurements in supine position correlated well with the measurements in upright position (Figure 2; Pearson correlation 0.74; P<0.01; 95% CI 0.64;0.82). CL measurements in upright position tended to be shorter (mean difference 1.9mm; SE 0.6mm; 95% CI 0.6;3.1mm) than the measurements taken in supine position. In supine position, funneling was present in 33 women (31%). In 6 out of these 33 women, funneling disappeared in the upright position, but in another 20 women funneling appeared only in the upright position. CL both in supine and upright position correlated with the Bishop Score (Figure 3; Pearson correlation -0.44; P<0.01; 95% CI -0.59;-0.27 and -0.45; P<0.01; 95% CI -0.60;-0.27, respectively), however correlation coefficients were rather low.

All parous women delivered vaginally, and were excluded from analysis for the risk of a CS for failure of progress. The ROC curves for the risk of a CS due to failure of progress in the nulliparous women are shown in Figure 4. The area under the curve was higher for the CL in supine and upright position than for the Bishop Score (0.66, 0.68 and 0.46 respectively). Logistic regression analysis showed that only the CL in upright position was a significant predictor of the risk of a CS (Table II). An increase of 1mm in CL was associated with a 14% increase in the odds of a CS for failure of progress.
The Bishop Score correlated significantly with the induction-to-delivery interval (Figure 5A - Pearson correlation -0.47; P<0.01; 95% CI -0.44;-0.28). However, when induction methods were analyzed separately, correlations were not significant for either oxytocin (Figure 5B) or prostaglandin induction (Pearson correlation -0.13; P=0.34 and -0.23; P=0.25, respectively). CL in either supine or upright position was not related to induction-to-delivery interval, irrespective of the induction method. Figure 6 shows the correlation between CL in supine and upright position for PGE2 and oxytocin induction (Pearson correlation 0.05; P=0.66; and 0.08; P=0.49, respectively).

Table I: Study characteristics

Demographic characteristics	*n (%)*	*Induction characteristics*	*n (%)*
Parity		Oxytocin induction	69 (65%)
Nulliparous	73 (68%)	Cervical length supine (mm, median (range))	22.1 (5.6-48.5)
Parous	34 (32%)	Cervical length upright (mm, median (range))	19.8 (4.6-39.7)
Ethnicity		Bishop Score (median (range))	7 (4-10)
Caucasian	104 (97%)	Prostaglandin induction	38 (35%)
Afro-Caribbean	2 (2%)	Cervical length supine (mm, median (range))	26.2 (11.5-43.1)
Asian	1 (1%)	Cervical length upright (mm, median (range))	25.1 (8.7-41.3)
Maternal age (years, median (range))	31 (21-41)	Bishop Score (median (range))	4 (1-8)
Gestational age (days, median (range))	285 (258-299)		
BMI (median (range))	25 (18-47)	Indication	
		Prolonged pregnancy	48 (45%)
		Hypertensive disorder	20 (19%)
		Diabetes	15 (14%)
		Prelabour rupture of membranes	6 (5%)
		Small for gestational age	6 (5%)
		Large for gestational age	3 (3%)
		Fetal distress	2 (2%)
		Obstetric history	2 (2%)
		Elective	5 (5%)
		Induction-to-delivery interval (hours, median (range))	6 (1-127)
		Modus partus	
		Vaginal delivery	91 (85%)
		Caesarean section for failure of progress	12 (11%)
		Caesarean section for fetal distress	4 (4%)

Table II: Logistic regression analysis for likelihood of caesarean section for nulliparous women

	Univariable analysis			*Multivariable analysis*		
Variable	*Odds ratio*	*95% CI*	*P*	*Odds ratio**	*95% CI*	*P*
CL supine	1.05	0.97;1.14	0.22	1.07	0.98;1.17	0.13
CL upright	1.10	1.00;1.20	0.04	1.14	1.02;1.27	0.02
Difference in CL	0.98	0.86;1.11	0.74			
% difference in CL	0.98	0.93;1.03	0.33			
Funneling supine						
Absent	1.00					
Present	0.70	0.17;2.92	0.63			
% Funneling	0.99	0.99;1.01	0.42			
Funnel width	0.98	0.94;1.03	0.47			
Funneling upright						
Absent	1.00					
Present	0.74	0.20;2.74	0.65			
% Funneling	1.00	0.98;1.01	0.49			
Funnel width	1.00	0.96;1.04	0.97			
Dilatation US						
Absent	1.00					
Present	0.60	0.12;3.14	0.55			
Bishop Score	1.12	0.77;1.64	0.56	1.00	0.64;1.58	0.99
Dilatation 0 cm	1.00					
Dilatation 1-2 cm	1.77	0.17;18.32	0.63			
Dilatation >2 cm	1.00	0.10;10.17	1.00			
Effacement 0	1.00					
Effacement ¼-½	1.15	0.11;11.78	0.90			
Effacement ≥ ¾	1.43	0.14;14.70	0.76			
Consistency firm	1.00					
Consistency medium	0.70	0.07;7.22	0.77			
Consistency soft	1.33	0.10;17.10	0.83			
Position posterior	1.00					
Midposition	3.02	0.56;16.33	0.20			
Position anterior	1.58	0.20;12.79	0.67			
Station Hodge 0	1.00					
Station Hodge 1	0.93	0.10;9.06	0.95			
Station ≥ Hodge 2	2.00	0.13;29.81	0.62			

* Odds ratio adjusted for fetal birthweight, gestational age at induction, prostaglandin use, maternal age and BMI ≥ 30

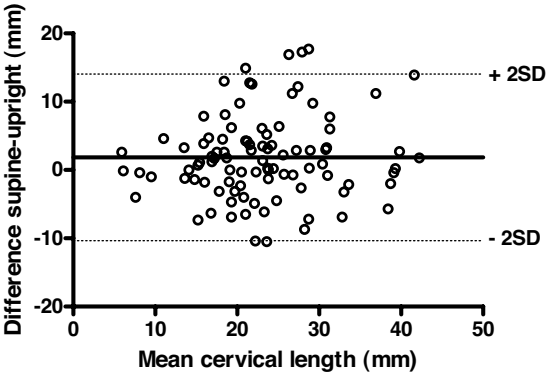

Figure 2: Bland-Altman plot of the difference between CL measurements in supine and upright position.

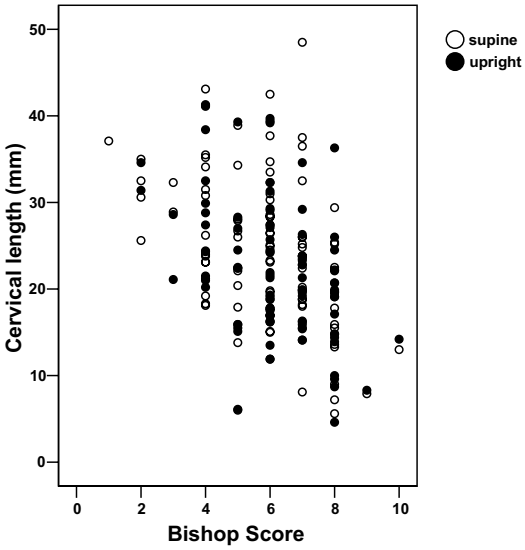

Figure 3: Correlation between CL measured in supine and upright position and the Bishop Score.

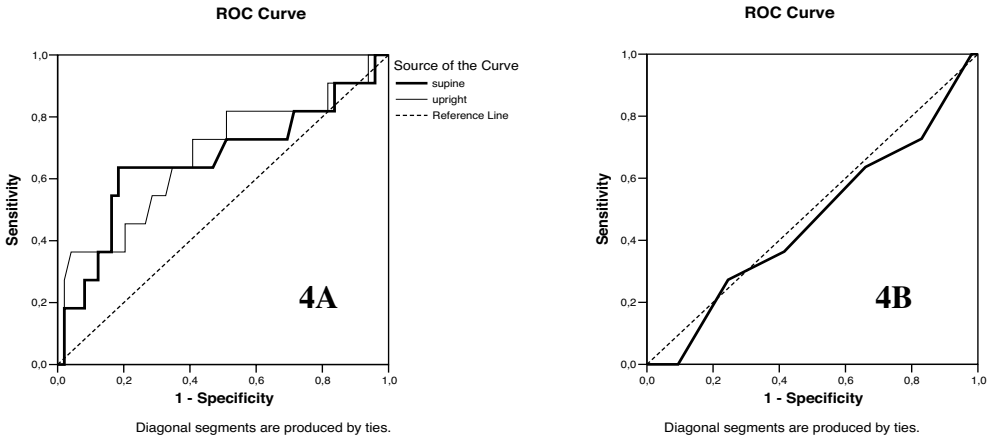

Figure 4: ROC curves of the CL in supine and upright position (4A) and Bishop Score (4B) for the risk of a caesarean section due to failure of progress.

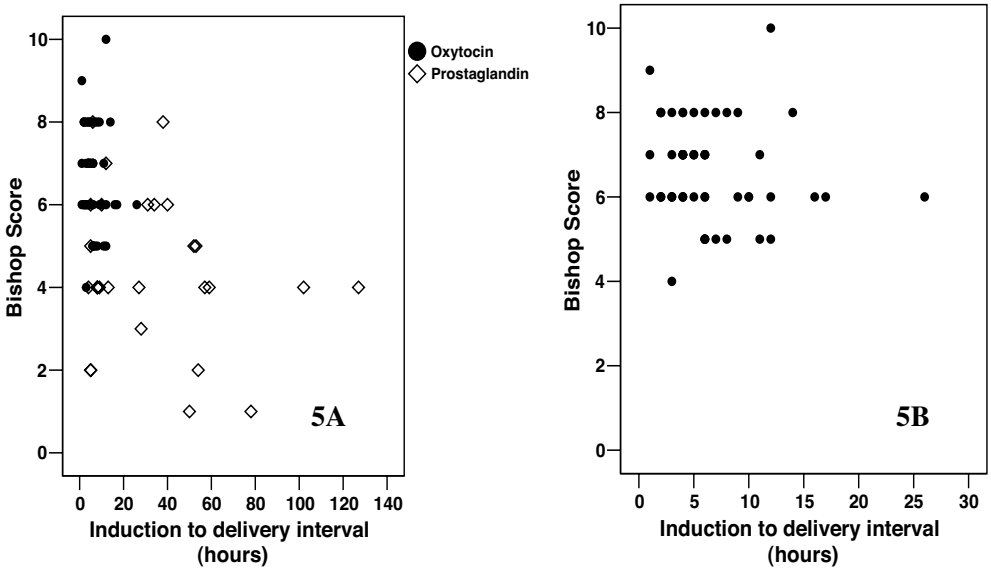

Figure 5: Correlation between Bishop Score and the induction-to-delivery interval (hours) for all inductions (5A) and only oxytocin inductions (5B).

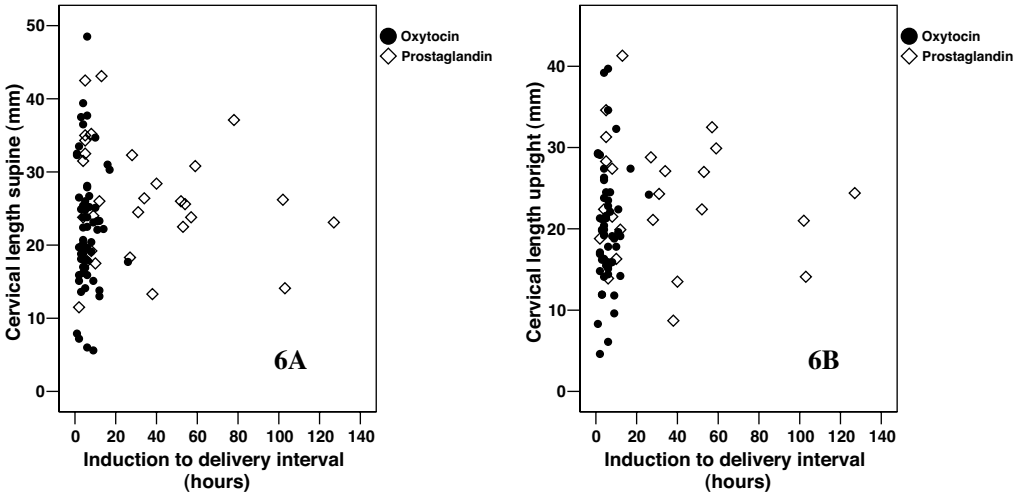

Figure 6: Correlation between CL in supine (6A) and upright position (6B), and the induction-to-delivery interval (hours).

Discussion

To the best of our knowledge, this is the first study in which the effect of a maternal postural change on the prediction of a successful induction of labour at term has been investigated. Our results demonstrate that the CL in upright position was the only significant predictor of a successful induction of labour, defined as a vaginal delivery. Both CL in supine and upright position were better predictors of a failed induction than the Bishop Score. However, none of the CL measurements were related to the induction-to-delivery interval. The Bishop Score was significantly related to the overall induction-to-delivery interval, but not to the induction-to-delivery interval for oxytocin or prostaglandin induction separately. The latter may be due to the fact that the Bishop Score was in general favourable for oxytocin inductions (median score 7), and unfavourable for prostaglandin inductions (median score 4), limiting the range over which a correlation could be established.

The fact that CL in upright position best predicted vaginal delivery, might be due to engagement of the head and subsequent CL changes in that position. It may be considered a functional test assessing disproportion (lack of engagement and CL changes) or otherwise. The Bishop Score, consisting of five different components is likely to represent cervical ripeness better than CL only, which may explain a better prediction of the duration of induction.

All previous studies that compared pre-induction sonographic CL measurements with the Bishop Score have used different definitions of a successful induction of labour and different

agents for induction of labour[13-30]. Therefore, overall conclusions are difficult to draw, with too few studies with sufficient data to perform a meta-analysis. However, some remarks can be made. In Table III we give an overview of the studies in which outcome of labour induction was related to pre-induction CL measurement and Bishop Score. Only studies in which success was defined as either a vaginal delivery, or as a vaginal delivery within 24 hours were selected. In 7 of the 9 studies sonographic CL was the best predictor of successful induction, when success was defined as a vaginal delivery. When a time factor was introduced in the definition of success, namely vaginal delivery within 24 hours, Bishop Score and CL measurement had a similar predictive value.

In conclusion, our results suggest that maternal postural change might improve the accuracy to predict of the outcome of labour induction at term. Furthermore, CL determined by TVS in both a supine and upright position appear to be stronger predictors of failed induction than the Bishop Score. This is in agreement with most of the literature. The Bishop Score may be a better predictor of the duration of labour, however the favourable results might have been biased since it was used for the selection of patients by the obstetricians in charge. Our results need to be confirmed in a larger and more homogeneous population.

Table III: Prediction of the outcome after labour induction
Cervical length (CL) versus Bishop Score (BS)

Success = Vaginal delivery					
	Sample size	CL Level of sign. OR (95% CI)	BS Level of sign. OR (95% CI)	Sens/Spec/PPV/NPV (Area Under the Curve)	Best predictor
Paterson-Brown 1991	50	n.s.	P=0.02	BS: 47/ 100 /100 /23	BS
Ware 2000	77	P<0.01 3.57†	n.s.		CL
Chandra 2001	122	n.s.	P<0.01 2.98 (1.71;5.20)	BS: 40/ 96/ 97/ 29	BS
Gabriel 2002	179	P<0.01	n.s.		CL
Rane 2003	382	P<0.01 1.13 (1.08;1.19)	n.s.	CL: (0.76) BS: (0.68)	CL
Daskalakis 2006	137	P<0.01	P=0.24	CL: (0.74) BS: (0.50)	CL
Peregrine 2006	267	P<0.01 1.07 (1.04;1.11)	n.s.		CL
Elghorori 2006	104	P<0.01 11.1†(2.4;50.0)	n.s.	CL: 62/ 100 (0.84) BS: 23/ 88 (0.50)	CL
Meijer *2007* *(present study)*	*73*	*1.07 (0.98;1.17)* *1.14 (1.02;1.27)*	*0.99 (0.64;1.58)*	*CL: (0.66/0.68)* *BS: (0.46)*	*CL upright*
Success = Vaginal delivery < 24 hours					
	Sample size	CL Level of sign. OR (95% CI)	BS Level of sign. OR (95% CI)	Sens/Spec/PPV/NPV (Area Under the Curve)	Best predictor
Gonen 1998	86	P<0.01	P<0.01	CL: 59/ 78/ 82/ 53 BS: 65/ 78/ 83/ 57	Similar
Pandis 2001	240	P<0.01 1.10 (1.06;1.12)	P=0.07 1.14 (0.99;1.31)		CL
Reis 2003	111	P<0.01	P<0.01	CL: 43/ 74/ 79/ 36 BS: 84/ 68/ 86/ 66	BS
Rane 2004	604	P<0.01 1.22 (1.18;1.28)	P<0.01 1.63 (1.47;1.81)	CL: 89/ 75 (0.89) BS: 68/ 75 (0.78)	CL
Bueno 2005	196	P<0.01 1.06 (1.02;1.11)	P<0.01 1.33 (1.14;1.59)	CL: (0.72) BS: (0.73)	Similar

† per cm CL n.s. = not significant OR=Odds Ratio

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7

Prediction of spontaneous onset of labour by transvaginal ultrasound of the cervix and Bishop Score at prolonged pregnancy

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Philip Stoutenbeek
Gerard H.A. Visser

Abstract

Introduction The aim of this study was to assess the chance of spontaneous onset of labour and risk of a caesarean section by transvaginal ultrasound examination of the cervix and Bishop Score in post term nulliparous women.

Methods Eighty five nulliparous women beyond 41 weeks of gestation underwent transvaginal ultrasound and digital examination of the cervix. Antenatal care was offered at least twice a week until 42 weeks of gestation, and thereafter at least at alternate days. Induction of labour was considered when a suboptimal fetal condition was assumed by any of the standard antenatal examinations or for maternal reasons.

Results The Bishop Score was a significant predictor of spontaneous onset of labour within 24, 48 and 96 hours from digital examination. Sonographic cervical length (CL) was only a significant predictor of spontaneous onset of labour within 96 hours from ultrasound examination, with a trend for spontaneous onset of labour within 48 hours. With a 30mm cut-off value, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for spontaneous onset of labour within 96 hours were 83%, 41%, 65% and 65%; and 73%, 59%, 69% and 64% for CL in supine and upright position, respectively. This was 49%, 80%, 78% and 51% for a Bishop Score larger than 5.

Conclusion Our results indicate that spontaneous onset of labour within 96 hours can be predicted at prolonged pregnancy by both digital examination and transvaginal ultrasound of the cervix. This information might be useful for both clinicians and patients who need to decide for either induction of labour or expectant management beyond 41 weeks of gestation.

Introduction

Approximately 5% of all pregnant women remain undelivered at 41 weeks of gestation[1]. Prolonged pregnancy is associated with an increase in perinatal mortality rate due to uteroplacental insufficiency, and with increased caesarean section (CS) rates[2]. Unfortunately, there is no evidence that fetal monitoring improves perinatal outcome in these cases[2].
There is still controversy about routine induction at 41 weeks of gestation. Advocates of this management have stated that the risks for mother and fetus have been underestimated. They state that the risk of a CS may even be lower when labour is induced as compared to expectant management[3-5]. However, others claim that these results are based on relative old studies with clinical management that differs from current practice, and that these studies report the occurrence of adverse outcomes without paying respect to the underlying cause[6].
With expectant management, approximately two third of all women beyond term will have spontaneous onset of labour before 42 weeks of gestation[7], and even more in case of a favourable cervix[8]. There is consensus that women beyond 41 weeks of gestation should be informed about the benefits and risks of expectant management and induction of labour. Information about the chance of spontaneous onset of labour within acceptable time would be a valuable consideration for the decision. The aim of this study was to estimate the likelihood of spontaneous onset of labour and the risk of a CS by transvaginal ultrasound and digital examination of the cervix in nulliparous women beyond 41 weeks of gestation.

Materials and methods

Nulliparous women beyond 41 weeks of gestation who attended the outpatient clinic from the University Medical Center, Utrecht, and the St. Antonius Hospital, Nieuwegein, The Netherlands, were asked to participate in the study between February 2004 and September 2006. Exclusion criteria were multiple gestation, non-cephalic presentation, and previous exconisation. Standard antenatal care consisted of ultrasound assessment of the Amnion Fluid Index (AFI), fetal heart rate monitoring, abdominal examination and digital examination of the cervix. Before digital examination and quantifying cervical ripeness by the modified Bishop Score (range 0-10)[9], transvaginal ultrasound of the cervix was performed by a sonographer, and clinicians were blinded for these results. The transvaginal ultrasound was performed as described previously[10], with an empty bladder and with avoidance of pressure on the cervix by the ultrasound probe. Cervical length (CL) measurements were taken with women in the supine position for at least 5 minutes. In a subgroup, the transvaginal ultrasound was repeated after a maternal postural change (n=60). CL measurements were taken when women were upright for at least 1 minute. The presence of funneling was defined

as opening of the internal os with herniation of the fetal membranes into the cervical canal. All measurements were performed by a 6-MHz endovaginal transducer (APLIO, Toshiba Medical Systems, Tokyo) or a 5-MHz endovaginal transducer (Aloka, Tokyo).

Antenatal care was offered at least twice a week until 42 weeks of gestation, and thereafter at least at alternate days. Induction of labour was considered when a suboptimal fetal condition was assumed by any of the antenatal examinations, or for maternal reasons.

Statistical analysis was performed with SPSS 12.0. When multiple ultrasound examinations were performed, only the first examination beyond 41 weeks of gestation was used for the analysis. The Pearson correlation coefficient was used to quantify the association between continuous variables, such as CL and Bishop Score. The difference of supine minus upright measured CL was depicted versus the mean CL in a Bland-Altman plot. The odds ratio for spontaneous onset of labour ≤42 weeks of gestation and within 24, 48 and 96 hours from ultrasound examination, and for the risk of a CS was calculated with logistic regression analysis. Fetal birthweight, labour induction, days to delivery, gestational age at delivery, maternal age and maternal BMI were considered as confounding factors for the risk of a CS, and were used in a multivariable logistic regression analysis. P values <0.05 were considered statistically significant.

The study was approved by the local Medical Ethics Committee. All women gave written informed consent.

Results

Eighty-five nulliparous women who were 41 to 42 weeks pregnant (mean 291 days) agreed to participate in the study. One third of the women had spontaneous onset of delivery before 42 weeks of gestation (Table I) and another 13 women beyond 42 weeks of gestation.

Table I: Study characteristics

Characteristics	*n (%)*
Parity	
Nulliparous	85 (100%)
Ethnicity	
Caucasian	80 (94%)
Afro-Caribbean	3 (4%)
Asian	2 (2%)
Maternal age (years, median (range))	31 (20-41)
BMI (median (range))	23 (18-51)
Gestational age at US (days, median (range))	291 (287-294)
CL supine (mm, median (range))	26.4 (6.5-52.6)
CL upright (mm, median (range))	25.3 (5.3-48.2)
Bishop Score (median (range))	5 (0-9)
Gestational age at delivery (days, median (range))	294 (289-300)
Spontaneous onset of delivery ≤ GA 42	30 (36%)
Induction ≤ GA 42	13 (15%)
Undelivered at GA 42^{+1}	42 (49%)
Mode of delivery	
Vaginal delivery	56 (66%)
CS for failure of progress	19 (22%)
CS for fetal distress	10 (12%)

CL was measured in supine and in 60 women also in upright position. There was a significant correlation between supine and upright measured CL (Pearson correlation 0.89; P<0.01; 95% CI 0.82;0.93) and the mean difference was small (mean difference 0.6mm; P=0.37; 95% CI 0.7;1.9mm). Both CL in supine position and in upright position were correlated significantly with the Bishop Score, but correlation coefficients were low (Pearson correlation -0.50; P<0.01; 95% CI -0.67;-0.29, Figure 1; and Pearson correlation -0.51; P<0.01; 95% CI -0.71;-0.23, respectively).

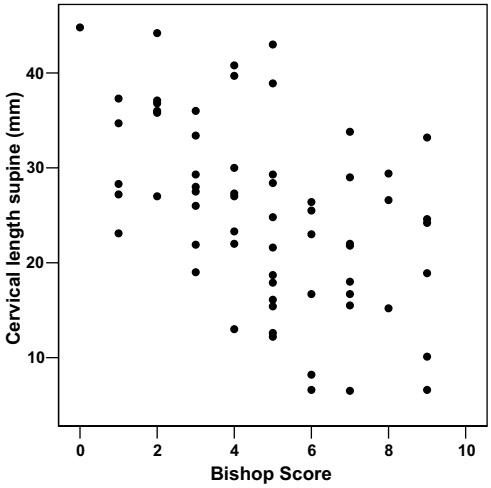

Figure 1: Correlation between CL measured in supine position and the Bishop Score.

Table II shows the logistic regression analysis for the risk of spontaneous onset of labour, either before 42^{+1} weeks of gestation, or within 24, 48 or 96 hours from the digital or ultrasound examination of the cervix. The Bishop Score was a significant predictor of spontaneous onset of labour within 24, 48 ad 96 hours from digital examination. Sonographic CL was only a significant predictor of spontaneous onset of labour within 96 hours from ultrasound examination, with a trend for the prediction of spontaneous onset of labour within 48 hours.

Figure 2 depicts the percentage of women with spontaneous onset of labour within 96 hours per CL subgroup (1-10, 11-20, 21-30, 31-40 and 41-50mm) and Bishop Score (0-2, 3-5 and >5). ROC curves indicated 30mm the optimal cut-off value for CL in both supine and upright position, and 5 for the Bishop Score. For these cut-off values, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were 83%, 41%, 65% and 65%; and 73%, 59%, 69% and 64% for CL in supine and upright position, respectively; and 49%, 80%, 78% and 51% for the Bishop Score.

Table III and IV show the logistic regression analysis for the risk of a CS and CS for failure of progress respectively. CL in upright position was the only variable that was significantly associated with the risk of CS, with presence of funneling being almost significant (P=0.06). However, neither CL, nor presence of funneling, nor the Bishop Score were indicative for labour outcome at prolonged pregnancy when adjusted for possible confounding factors.

Table II: Logistic regression analysis for spontaneous onset of labour

	Univariable analysis		
≤ GA 42	***Odds ratio***	***95% CI***	***P***
CL supine	0.97	0.92;1.02	0.23
Funneling supine			
Absent	1.00		
Present	1.25	0.37;4.18	0.72
CL upright	0.94	0.89;1.00	0.05
Funneling upright			
Absent	1.00		
Present	0.53	0.14;1.98	0.34
Bishop Score	1.22	0.95;1.56	0.12
≤ 24 hours			
CL supine	0.98	0.92;1.05	0.58
Funneling supine			
Absent	1.00		
Present	0.38	0.04;3.31	0.38
CL upright	0.98	0.92;1.04	0.49
Funneling upright			
Absent	1.00		
Present	0.65	0.12;3.60	0.62
Bishop Score	1.89	1.15;3.08	0.01
≤ 48 hours			
CL supine	0.95	0.90;1.01	0.08
Funneling supine			
Absent	1.00		
Present	2.11	0.56;7.97	0.27
CL upright	0.95	0.89;1.01	0.09
Funneling upright			
Absent	1.00		
Present	0.80	0.18;3.59	0.77
Bishop Score	1.49	1.07;2.07	0.02
≤ 96 hours			
CL supine	0.92	0.87;0.98	<0.01
Funneling supine			
Absent	1.00		
Present	1.69	0.46;6.25	0.43
CL upright	0.91	0.86;0.97	<0.01
Funneling upright			
Absent	1.00		
Present	0.56	0.14;2.23	0.41
Bishop Score	1.46	1.07;1.98	0.02

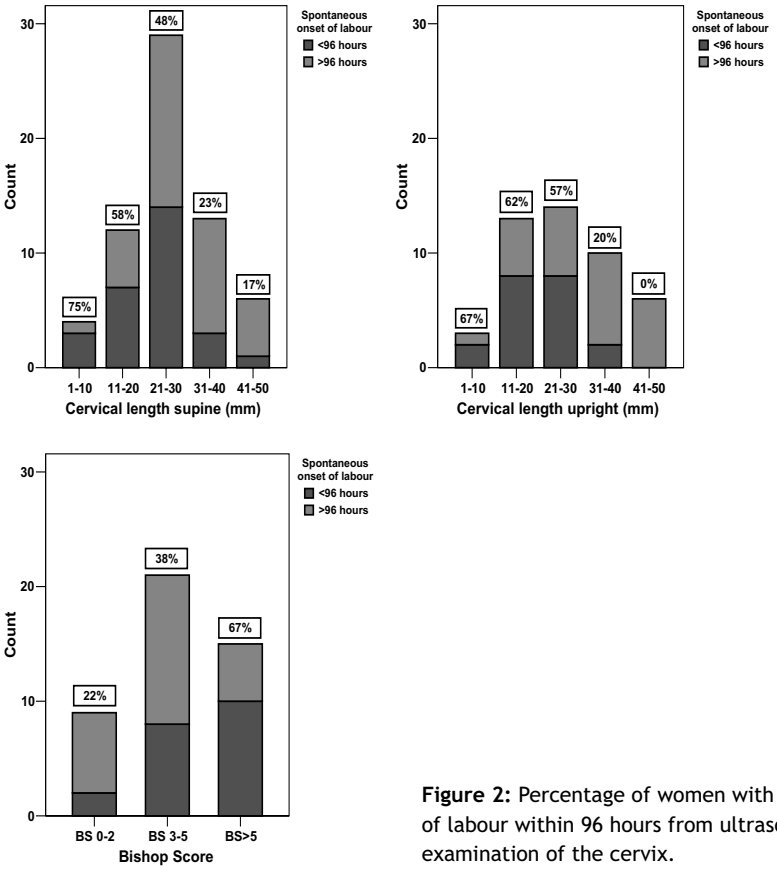

Figure 2: Percentage of women with spontaneous onset of labour within 96 hours from ultrasound or digital examination of the cervix.

Table III: Logistic regression analysis for the risk of a CS

	Univariable analysis			*Multivariable analysis*		
Variable	*Odds ratio*	*95% CI*	*P*	*Odds ratio**	*95% CI*	*P*
CL supine	1.03	0.99;1.08	0.17	1.04	0.97;1.11	0.32
Funneling supine						
Absent	1.00			1.00		
Present	0.22	0.05;1.06	0.06	2.24	0.42;11.97	0.34
CL upright	1.07	1.01;1.12	0.02	1.05	0.97;1.14	0.21
Funneling upright						
Absent	1.00			1.00		
Present	0.47	0.13;1.69	0.25	0.62	0.11;3.60	0.60
Bishop Score	0.90	0.72;1.13	0.37	0.95	0.69;1.31	0.75

*** Odds ratio adjusted for fetal birthweigth, labour induction, days to delivery, gestational age at delivery, maternal age and BMI ≥ 30.**

Table IV: Logistic regression analysis for the risk of a CS for failure of progress

	Univariable analysis			*Multivariable analysis*		
Variable	*Odds ratio*	*95% CI*	*P*	*Odds ratio**	*95% CI*	*P*
CL supine	1.02	0.97;1.08	0.45	1.04	0.95;1.14	0.35
Funneling supine						
Absent	1.00			1.00		
Present	0.17	0.02;1.37	0.10	0.22	0.02;2.10	0.19
CL upright	1.05	0.99;1.11	0.11	1.05	0.96;1.16	0.28
Funneling upright						
Absent	1.00			1.00		
Present	0.50	0.12;2.09	0.34	0.43	0.08;2.28	0.32
Bishop Score	1.03	0.79;1.35	0.84	1.10	0.73;1.64	0.66

*** Odds ratio adjusted for fetal birthweigth, labour induction, days to delivery, gestational age at delivery, maternal age and BMI ≥ 30.**

Discussion

Our results indicate that both digital examination and transvaginal ultrasound of the cervix can predict spontaneous onset of labour within 3 days in nulliparous women beyond 41 weeks of gestation. These data confirm a recent study by Strobel et al[11], who found sonographic CL and Bishop Score equally predictive of spontaneous onset of labour at prolonged pregnancy in nulliparous (n=45) and parous (n=52) women. Both studies are hampered by the fact that the populations were relatively small (85 and 45 nulliparous women respectively) and should therefore be confirmed in larger populations.

Induction of labour increases the risk of CS compared to spontaneous onset of labour[12;13]. At prolonged pregnancy, nulliparous women have a higher risk of a failed induction[14-16] and prolonged labour[17] than parous women, and this risk is further increased by an unfavourable cervix[15;16], unengaged vertex[18], and epidural use during labour[16]. CS rates appear to be increased by these intrinsic factors rather than by induction of labour itself[16].

These aspects, together with the increased risk of perinatal mortality beyond term age, are in favour of induction of labour. However, identification of women in whom spontaneous labour is about to start, may prevent unnecessary inductions. Risk assessment should be individualized and the possibility of spontaneous onset of labour within acceptable time should be taken in consideration and discussed with the patient. In our population about 75% of women had a CL smaller than 30mm and in about two-third of them labour indeed started within 96 hours. In case of a more unfavourable cervix, the likelihood of spontaneous onset of labour within 96 hours was less than 30%. The rather low predictive value can be explained by the large variation in CL and in CL changes preceding spontaneous labour. In a previous longitudinal observational study[19], we found CL shortening in about half of patients

in the weeks preceding spontaneous onset of labour, whereas in the other half no shortening had occurred until shortly before labour. Two-third of the latter group had a CL larger than 30mm in the last week preceding spontaneous onset of labour and even 24% of the women had a CL ≥30mm in the last 48 hours. So, ranges in physiology of CL and CL changes preceding spontaneous onset of labour are large.

CL in upright position was the only single variable that was significantly associated with the risk of a CS. This also confirms earlier findings from our group[20]. CL measurement in upright position may be considered a functional test assessing disproportion (lack of engagement and CL changes) or otherwise.

In conclusion, our results indicate that spontaneous onset of labour within 96 hours can be predicted at prolonged pregnancy by both digital examination and transvaginal ultrasound of the cervix. This information is useful for both clinicians and patients who need to decide for either induction of labour or expectant management beyond 41 weeks of gestation. However, the predictive value of these measurements regarding spontaneous onset of labour is not high.

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8

Prediction of the mode of delivery in women with a previous caesarean section by transvaginal sonography of the cervix

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Gerard H.A. Visser

Abstract

Introduction Information about the likelihood of vaginal birth after caesarean section (CS) would be helpful in counselling women with a previous CS on the route of delivery. The aim of this pilot study was to attempt to predict the mode of delivery in women with a previous CS by transvaginal ultrasound of the cervix.

Methods Women with one previous CS for either failure of progress or breech presentation underwent sonographic cervical length (CL) measurements at weekly intervals from 36 weeks of gestation until delivery.

Results Thirty six women with one previous CS were included. Women with a previous CS for failure of progress delivered by CS more frequent than the women with a previous elective CS for breech presentation (53% and 20%, respectively). This difference was mainly due to the elective CS. Approximately 80% of women undergoing trial of labour (TOL) delivered vaginally in both groups. The risk of a CS could not be predicted by the ultrasound parameters, neither at 37 weeks of gestation, nor at 40 weeks of gestation, nor within 7 days to delivery. Spontaneous onset of labour before 41 weeks of gestation could be predicted by a single CL measurement at 37 weeks of gestation, but only in the women with a previous CS for breech presentation.

Conclusion The ultrasound parameters were not predictive for the likelihood of a repeat CS. However, the study is hampered by the small number of patients, and should be repeated in a larger population.

Introduction

In the last decade, caesarean section (CS) rates have increased in the Netherlands, and women with a singleton fetus in vertex position between 37 and 42 weeks of gestation contribute most to the absolute CS rate[1]. Women with a previous CS undergoing trial of labour (TOL) are exposed to the risk of a uterine rupture. This is associated with considerable maternal and perinatal morbidity and a 2-14% perinatal mortality rate[2-6]. Elective repeat CS may well reduce maternal and neonatal morbidity compared to a repeat CS after failed TOL[7;8].

Information about the likelihood of vaginal birth after caesarean section (VBAC) would be helpful in counselling women with a previous CS on the route of delivery. Variables that are associated with VBAC are the indication for the previous CS, birth weight or gestational age at the previous CS, or a history of at least one vaginal delivery or VBAC[9]. At the onset of labour, a favourable cervix at digital examination and gestational age under 41 weeks of gestation are associated with VBAC[9]. At pre-induction evaluation of the cervix at term, transvaginal ultrasound appears to be a better predictor of a vaginal delivery than digital examination[10]. The aim of this study was to predict the mode of delivery in women with a previous CS by transvaginal ultrasound of the cervix.

Materials and methods

Women with one previous CS for either failure of progress or breech presentation were recruited at the University Medical Center, Utrecht, The Netherlands, and at the Hospital Oost-Limburg, Genk, Belgium, between February 2004 and September 2006. Exclusion criteria were multiple pregnancy, non-cephalic presentation, previous vaginal delivery, admission for threatened preterm labour and previous exconisation of the cervix. Sonographic cervical length (CL) measurements were taken at weekly intervals from 36 weeks of gestation onwards. The CL was measured by transvaginal ultrasound (6-MHz endovaginal transducer, APLIO, Toshiba Medical Systems, Tokyo; 7.5-MHz endovaginal transducer- Esaote Aquila, Genova, Italy). Women were in supine position and emptied the bladder before the ultrasound examination. The transvaginal ultrasound probe was withdrawn until a sagittal view of the cervix was obtained without distortion of the shape by pressure of the ultrasound probe. CL was measured from the internal to the external os, with a clear view of the cervical canal. Funneling was considered present when funnel length, measured from the internal os to the fetal occiput, was more than 5mm. The examination was repeated with the women in upright position, at least 1 minute after the postural change.

Statistical analysis was performed with SPSS 12.0. The odds ratio for the risk of a caesarean section was analyzed by a logistic regression analysis. The difference in gestational age

at delivery between women who delivered vaginally after TOL and women who had a CS was analyzed by the Mann-Whitney U test. A ROC curve was performed to determine the optimal cut-off value for the prediction of spontaneous onset of labour by a transvaginal CL measurement at 37 weeks of gestation. P values <0.05 were considered statistically significant.
The study was approved by the local Medical Ethics Committee, and all women gave written informed consent.

Results

Thirty six women with one previous CS were included in the study. Nineteen women (53%) had a previous CS for failure of progress, and 17 (47%) had an elective CS for breech presentation. Patient characteristics are shown in Table I.

Table I: Study characteristics

Characteristics	*n (%)*
Previous CS	36 (100%)
Failure of progress	19 (53%)
Breech presentation	17 (47%)
Ethnicity	
Caucasian	34 (94%)
Afro-Caribbean	1 (3%)
Negroid	1 (3%)
Maternal age (years, median (range))	33 (26-45)
BMI (median (range))	22 (18-41)
Gestational age at delivery (days, median (range))	281 (270-292)
Spontaneous onset of labour	21 (58%)
Vaginal delivery	16 (76%)
CS for failure of progress	3 (14%)
CS for fetal distress	1 (5%)
Elective CS	1 (5%)
Induction of labour	5 (14%)
Vaginal delivery	5 (100%)
Elective CS	10 (28%)

Women with a previous CS for failure of progress delivered by CS more frequent than the women with a previous elective CS for breech presentation (53% and 20%, respectively – Figure 1). This difference was mainly due to differences in elective CS's. Approximately 80% of women undergoing TOL delivered vaginally in both groups.

The risk of a CS could not be predicted by the ultrasound parameters, neither at 37 weeks of gestation, nor at 40 weeks of gestation, nor within 7 days to delivery although CL in supine position tended to be longer in women requiring a CS within 7 days (Table II; P=0.12). Funneling being present in the last 7 days prior to delivery tended to increase the chance of a CS. However, only 6 women had funneling present on transvaginal ultrasound, resulting in a large confidence interval. Therefore, this is not clinically relevant. The only significant predictor of outcome of labour was gestational age (GA). GA at delivery was significantly higher in women who had an elective CS than in women who delivered vaginally after TOL (Figure 2; Mann-Whitney U test, P=0.02). The indications for the elective CS are shown in Table III. Seven women (64%) were beyond 41 weeks of gestation, and in 5 women (45%) GA in combination with an unfavourable cervix were the only indications for elective CS.

Table II: Logistic regression analysis for the risk of a CS

	Univariable analysis		
Variable	*Odds ratio*	*95% CI*	*P*
Supine			
CL at GA 37	1.01	0.95;1.08	0.78
Funneling at GA 37			
Absent	1.00		
Present	1.06	0.20;5.64	0.94
CL at GA 40	1.02	0.95;1.10	0.55
Funneling at GA 40			
Absent	1.00		
Present	2.22	0.33;15.18	0.42
CL < 7 days to delivery	1.06	0.99;1.14	0.12
Funneling < 7 days to delivery			
Absent	1.00		
Present	2.08	0.44;9.84	0.35
Upright			
CL at GA 37	1.00	0.93;1.08	0.96
Funneling at GA 37			
Absent	1.00		
Present	3.78	0.58;24.75	0.17
CL at GA 40	1.03	0.95;1.13	0.49
Funneling at GA 40			
Absent	1.00		
Present	1.25	0.22;7.08	0.80
CL < 7 days to delivery	0.97	0.90;1.05	0.43
Funneling < 7 days to delivery			
Absent	1.00		
Present	4.67	0.87;25.14	0.07
GA at delivery	1.11	1.00;1.25	0.06
Birthweight	1.00	1.00;1.00	0.15
Maternal age	1.07	0.92;1.24	0.40
BMI	1.05	0.91;1.20	0.52

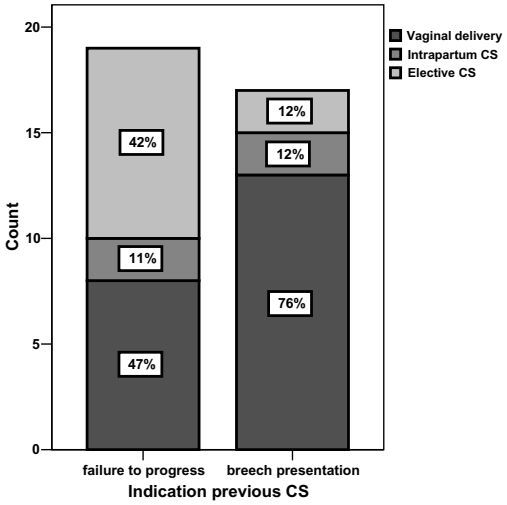

Figure 1: Mode of delivery for women with a previous CS for either failure of progress or breech presentation.

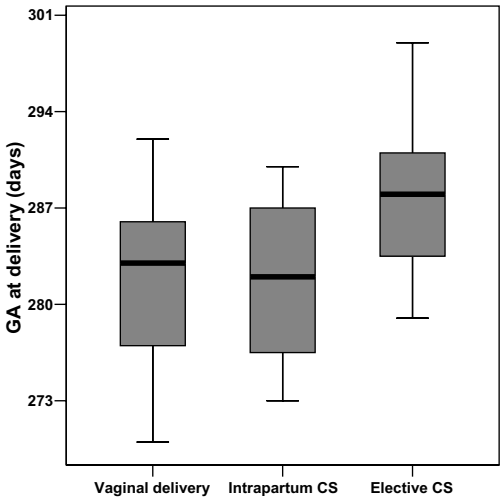

Figure 2: Boxplot of the gestational age at delivery according to the outcome of labour.

Table III: Indications for elective CS

nr.	*GA (days)*	*Indication*
1.	280	Hypertension and unfavourable cervix
2.	281	Abnormal CTG and no dilation
3.	287	Maternal request
4.	291	Gestational age and unengaged vertex
5.	296	Gestational age and unengaged vertex
6.	286	Obstetric history and macrosomia
7.	299	Gestational age and unfavourable cervix
8.	291	Obstetric history and unengaged vertex and macrosomia
9.	280	Unstable fetal position
10.	288	Gestational age and unfavourable cervix
11.	290	Gestational age and unfavourable cervix

Since a considerable part of women with a previous CS for failure of progress delivered by elective CS, and since the majority of these women were beyond 41 weeks of gestation, we investigated the prediction of prolonged pregnancy by transvaginal ultrasound of the cervix. The ROC curve of a CL measurement in supine position at 37 weeks of gestation indicated 38mm and 30mm as the optimal cut-off value for women with a previous CS for failure of progress and for breech presentation, respectively (Figure 3). For these cut-off values, the positive predictive value (PPV) for spontaneous onset of labour before 41 weeks of gestation were 56% and 83% respectively (sensitivity 50%; specificity 56%; PPV 56%; NPV 50% and sensitivity 42%; specificity 80%; PPV 83%; NPV 36%, respectively - Figure 4). CL in upright position was not useful for the prediction of spontaneous onset of labour before 41 weeks of gestation (Area Under the Curve 0.50).

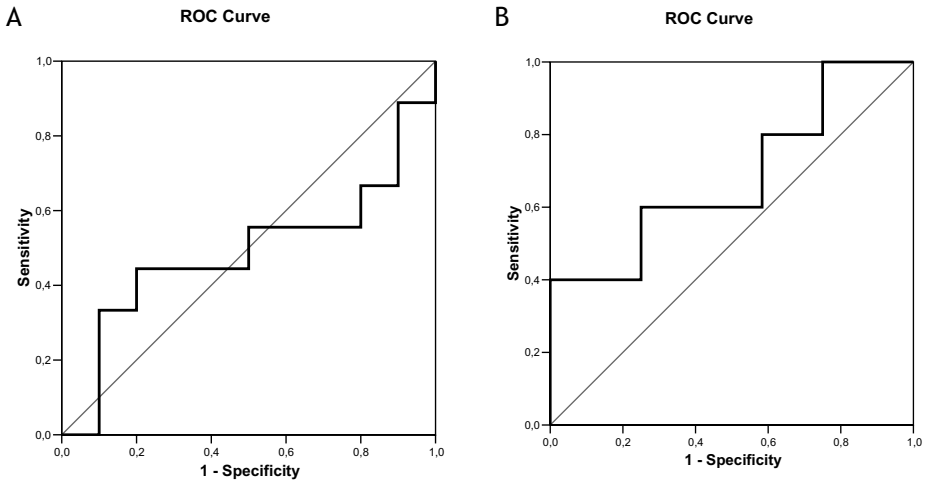

Figure 3: ROC curve for the prediction of spontaneous onset of labour before 41 weeks of gestation by a transvaginal CL measurement in supine position at 37 weeks of gestation for women with a previous CS for failure of progress (3A) and for breech presentation (3B).

4A	Spontaneous onset of labour before 41 weeks of gestation		Total
	Yes	**No**	
Cervical length < 38 mm	5	4	9
Cervical length ≥ 38 mm	5	5	10
Total	10	9	19

4B	Spontaneous onset of labour before 41 weeks of gestation		Total
	Yes	**No**	
Cervical length < 30 mm	5	1	6
Cervical length ≥ 30 mm	7	4	11
Total	12	5	17

Figure 4: 2 x 2 contingency table for the prediction of spontaneous onset of labour before 41 weeks of gestation by a CL measurement at 37 weeks of gestation for women with a previous CS for failure of progress (4A) and for breech presentation (4B).

Discussion

Our data indicate that women with a previous CS for failure of progress are most likely to deliver by repeat CS after 41 weeks of gestation. Apparently, in these women spontaneous labour is less likely to occur in time. In 47% (9 out of 19) labour had not started at 41 weeks of gestation and this contrasts the 5% in unselected populations in which gestational age was determined by early ultrasound[11]. Unengaged vertex, unstable fetal position and unfavourable cervix were the most common reasons for these CS's. Approximately 80% of all TOL resulted in a vaginal delivery, which is in agreement with previous literature[12;13]. The likelihood of a repeat CS could not be predicted by the ultrasound parameters, with only a weak trend for CL within 7 days before delivery.

Previously, it has been reported that the risk of a CS can be predicted by a single sonographic CL at 37 weeks of gestation in both nulliparous and parous women[14]. Furthermore, sonographic CL can predict spontaneous onset of delivery within 7 days at term[15;16], and identify women who are at increased risk for prolonged pregnancy[14;17]. In the present study, the ultrasound parameters were not predictive for the mode of delivery, but this may be due to the limited number of patients that could be included. In a previous study, we found CL in upright position to be the best predictor of the mode of delivery after induction of labour at term[10]. Measuring CL after a maternal postural change may be considered a functional test assessing disproportion (lack of engagement of the fetal occiput and subsequent CL changes). In the present study, a maternal postural change test was not helpful in predicting the mode of delivery.

Spontaneous onset of labour before 41 weeks of gestation could only be predicted by a single CL measurement in supine position at 37 weeks of gestation in the group of women with a previous CS for breech presentation. Although this might be coincidental because of the limited number of patients (n=17), we found a similar cut-off point for CL and similar predictive values in a large population of nulliparous women at term[17]. Women who had a previous elective CS for breech presentation may resemble nulliparous women, whereas women with a previous CS for failure of progress had dilatation of the cervix and may be considered parous women. The cut-off value for CL in the group of women with a previous CS for failure of progress was higher than for women with a previous CS for breech presentation, which is in agreement with literature regarding differences between nulliparous and parous women[14].

In conclusion, the difference in repeat CS rate between women with a previous CS for failure of progress and for breech presentation was mainly caused by the number of elective CS for women with a previous CS for failure of progress beyond 41 weeks of gestation. After TOL the likelihood of a vaginal delivery was 80% in both groups. The ultrasound parameters were only predictive for spontaneous onset of delivery before 41 weeks of gestation in the group of women with a previous CS for breech presentation. In both groups the likelihood of

a repeat CS could not be predicted by transvaginal ultrasound of the cervix. However, these results are based on a low number of patients, and firm conclusions can only be drawn when the study is repeated in a larger population.

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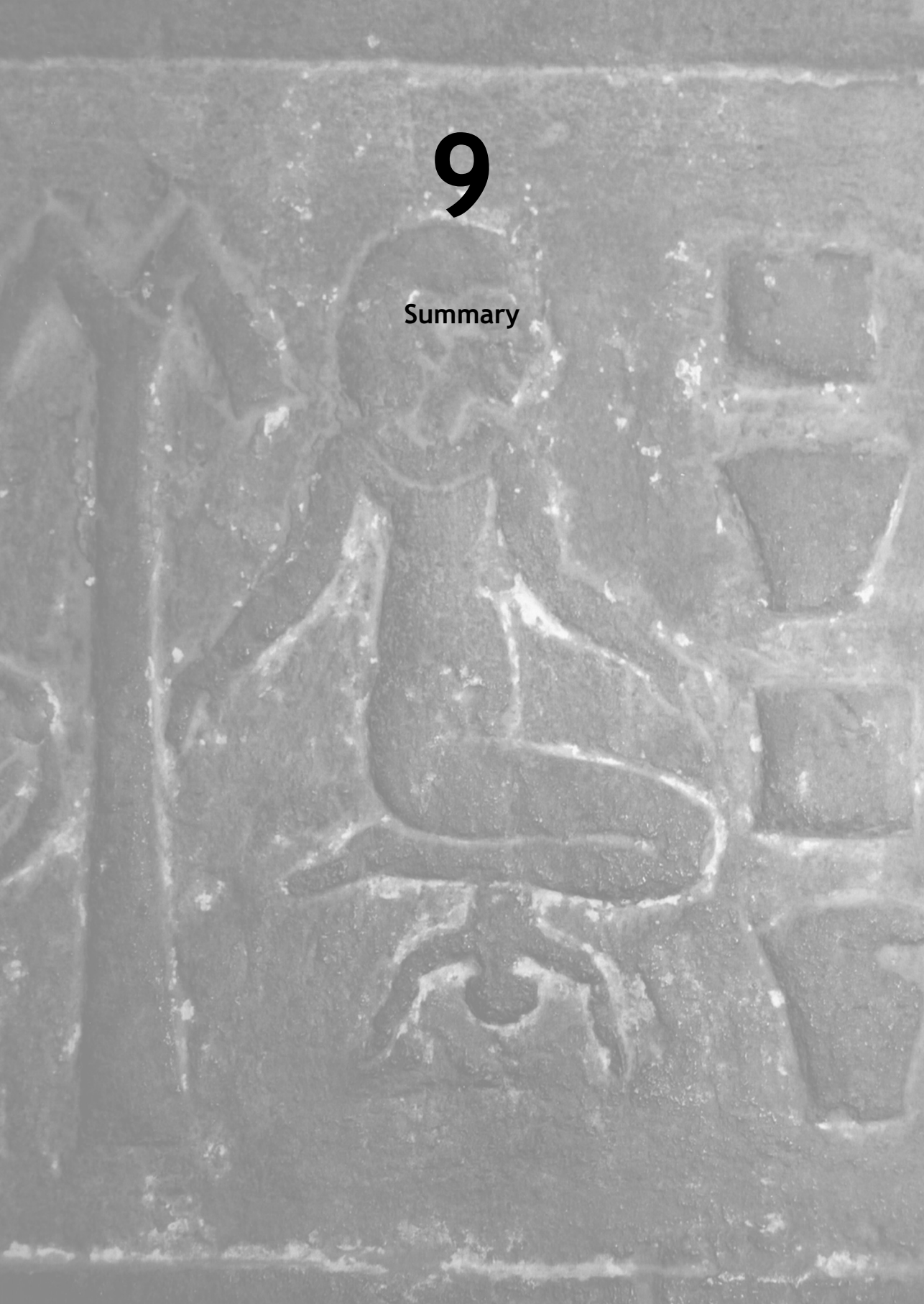
9

Summary



Summary

In this thesis the cervix is investigated by transvaginal sonography (TVS) at term to obtain more insight in physiological changes preceding parturition and to relate these changes or otherwise to the onset and course of spontaneous labour and to the need for and outcome of induced labour. TVS of the cervix is nowadays widely used as a diagnostic tool for the detection of threatened preterm labour. However, there is only limited information on physiology of the cervix at term.

This thesis aimed to answer the following questions:

1-What is the "gold standard" to obtain optimal cervical measurements, which are the pitfalls and what is the relevance of the different cervical parameters?

2-What are the fluctuations in cervical length (CL) and which factors cause such fluctuations?

3-How reliable are transperineal CL measurements at term gestation?

4-Does the cervix change preceding spontaneous onset of labour at term and can the timing of labour be predicted by CL measurements or by changes in CL with time?

5-Can pre-induction CL measurements in either supine or upright position predict the outcome of labour induction at term better than the Bishop Score?

6-Can TVS of the cervix or the Bishop Score predict spontaneous onset of labour beyond 41 weeks of gestation?

7-Can women at high risk for a repeat caesarean section (CS) be detected by serial CL measurements?

In *chapter 2* we compared different techniques of cervical sonography and investigated factors that influence visualization of the cervix, by reviewing the literature. There are three frequently used approaches, namely transabdominal, transperineal and transvaginal sonography of the cervix. With transabdominal sonography, a full bladder is necessary to adequately visualize the cervix[1]. However, this is known to artificially elongate the cervix[2;3]. Identification of the landmarks of the cervix, the internal and external os and the cervical canal, is often difficult in case of a short cervix[1]. The transperineal approach has the disadvantage that the cervix may be obscured by shadowing from the bowel gas or the pubic symphysis[4]. Images may be improved by elevation of the hips, however, failure to obtain a clear image of the cervix has been reported in up to 12% of cases and is dependent on the experience of the investigator[5-11]. TVS of the cervix has to be considered the gold standard. Clear images can be obtained in nearly 100% of the cases and the method is easy to learn even for inexperienced investigators[12]. It is a reproducible method[13-15], at least when measurements are taken with an empty bladder and pressure on the cervix by the transvaginal probe is avoided. When the cervix is curved, CL is measured in a straight line

from the internal to the external os[16]. Funneling can be present and may be considered physiological during the third trimester of pregnancy[17;18]. At midgestation, the presence of a funnel increases the risk of preterm delivery in both high risk[19-21] (OR 5.61; 95% CI 4.40;10.58) and low risk women[22;23] (OR 9.44; 95% CI 8.30;10.58). The shape of the funnel is often variable during TVS examination and measurement of funnel dimensions may falsely suggest precision[24]. The funnel may be masked when measured in supine position only[24-28]. Provocation tests such as transfundal pressure or TVS in standing position should be performed when funneling is absent in women at high risk for preterm delivery, to avoid missing the right diagnosis.

Spontaneous changes of the cervix have been reported previously[21;24;28]. In *chapter 3* we investigated the factors that influence the appearance of the cervix by performing continuous TVS of the cervix for 30 minutes in 6 nulliparous women and 12 parous women, who were equally divided in either at high or low risk for preterm delivery. The examination was performed once between 23 and 40 weeks of gestation. One woman delivered at 34 weeks of gestation, all other women beyond 36 weeks of gestation. The overall mean difference between the shortest and longest measured CL during the 30 minute examination was 10.9mm (range 1.6-22.0mm). In some women alterations in the cervical shape were associated with fetal movements and peristalsis of the bowel. We demonstrated that dynamic changes in CL can already be present at early gestation and long before delivery. However, the study was limited by the small number of patients and the wide range of gestional age at ultrasound examination. Therefore, the predictive value of these dynamic changes for spontaneous onset of either preterm or term labour can not be concluded from these preliminary results. The fact that large fluctuations exist in CL implies that clinical decisions can not be made on a single CL measurement. Repeated CL measurements give information about the amount of fluctuations, however the clinical significance of these fluctuations is unclear and needs further investigation.

Transperineal sonography of the cervix appears to be a reliable substitute for TVS in the preterm period of pregnancy, when performed by an experienced investigator[5-11]. In *chapter 4* we investigated its reliability and acceptability in the third trimester of pregnancy and compared the results with mid-gestation ultrasound examinations. CL measured by transperineal sonography correlated well with TVS in the third trimester (Pearson correlation 0.79; 95% CI 0.63;0.88) and even better at mid-gestation (Pearson correlation 0.94; 95% CI 0.82;0.98). However, in 19% and 30%, respectively, we failed to obtain a clear image of the cervix with transperineal sonography, due to shadowing and the limited experience of our sonographers with the transperineal technique. Previously, it has been reported that the percentage of failures can be reduced considerably -from 55 to 12%- after an initial learning period of 200 transperineal scans[7]. Our sonographers appreciated the transvaginal images

of the cervix better than the transperineal images, especially at mid-gestation. In the third trimester, a cephalic position of the fetus was helpful in identifying the landmarks -the internal and external os and the cervical canal- of the cervix. Most women (68%) valued transperineal sonography not or only mildly painful. However, in general, transperineal sonography was valued more painful than TVS (Wilcoxon signed rank test; P=0.01). We concluded that transperineal sonography by an experienced sonographer can be a feasible alternative for TVS of the cervix in the third trimester of pregnancy. Success rates of obtaining a clear image appear to improve with advanced gestation due to facilitated identification of the cervical landmarks by engagement of the fetal occiput.

In *chapter 5* we aimed to obtain insight in physiological changes of the cervix preceding term parturition by performing serial TVS of the cervix from 36 weeks of gestation onwards in 162 nulliparous women. TVS of the cervix was performed at weekly intervals in supine and upright maternal position. Supine and upright measured CL correlated well (Pearson correlation 0.90; 95% CI 0.84;0.94). The last CL measurement prior to delivery was correlated significantly with the ultrasound-delivery interval, although the correlation coefficient was low (range 0-12 days; Pearson correlation -0.26; 95% CI -0.45;-0.05). In 31% of women, the last CL prior to delivery was larger than 30mm. When CL was observed in serial individual plots, we found that in half of the population either a sudden decrease in CL in the last 2 weeks prior to delivery occurred, or a gradual decrease in CL over more than 2 weeks. These patterns have been described before in two small studies[17;18]. However, in the other 50%, CL remained unchanged until shortly -maximum 7 days- before delivery. A single CL measurement less than 30mm at 37 weeks of gestation in either supine or upright position appeared to predict spontaneous onset of labour before 41 weeks of gestation, but with low sensitivity and negative predictive value (sensitivity 46% and 53%; specificity 78% and 72%; PPV 82% and 81%; and NPV 40% and 40%, respectively). In conclusion, inter-individual variation in CL and in CL changes preceding spontaneous onset of labour are large. This hampers prediction of the onset of labour and must be taken into consideration with the interpretation of single or repeated CL measurements.

Nulliparity is associated with a longer duration of induced labour and a higher risk of failed induction[29;30]. The prediction of failed induction by pre-induction sonographic CL or Bishop Score has been investigated previously. Comparison of the different studies is hampered by the fact that different definitions of failed induction and different induction agents were used. In *chapter 6* we investigated the predictive value of pre-induction CL and Bishop Score for a successful outcome of labour induction at term. Success was defined as a vaginal delivery. A materal postural change has been shown to improve the accuracy of risk assessment of preterm birth[31;32]. Therefore, we aimed to improve the accuracy of risk assessment of failed induction at term by a maternal postural change. At logistic regression

analysis, CL in upright position was the only significant predictor of a vaginal delivery after induction of labour in nulliparous women at term (OR 1.14; 95% CI 1.02;1.27). Both CL in supine and upright position were better predictors of failed induction than the Bishop Score. The Bishop Score was the best predictor of duration of labour. Also in literature CL generally was found to be the best predictor of vaginal delivery, but with low sensitivity and NPV[33-40]. When the duration of labour is introduced in the definition of success, namely a vaginal delivery within 24 hours, then the Bishop Score appears to be an equally good predictor of failed induction as the CL[41-45]. This might be explained by the fact that the Bishop Score consists of five different aspects of the cervix, and may reflect cervical ripeness better than CL only. CL in upright position may be considered as a functional test, assessing disproportion that may result in lack of engagement of the fetal occiput and subsequent CL changes. This might explain the fact that CL in upright position was the best predictor of a vaginal delivery.

There is consensus that women beyond 41 weeks of gestation should be informed about the risks and benefits of expectant management as compared to induction of labour. Especially in nulliparous women, who have an increased the risk of failed induction[30;39;46] and prolonged labour[47], identification of those in whom spontaneous labour is about to start may reduce unnecessary inductions. In *chapter 7* we performed transvaginal CL measurements and digital examination of the cervix in 85 nulliparous women beyond 41 weeks of gestation and investigated the predictive value for spontaneous onset of labour. Spontaneous onset of labour within 96 hours from digital or ultrasound examination was predicted by a Bishop Score >5 and a CL ≤30mm (OR 1.46; 95% CI 1.07;1.98; and OR 0.92; 95% CI 0.87;0.98, respectively), which confirms previous results[48]. A maternal postural change did not contribute to the prediction of spontaneous onset of labour, however CL in upright position was the only significant predictor of the risk of a CS (OR 1.07; 95% CI 1.01;1.12). Again, this might be explained by the fact that the Bishop Score may reflect cervical ripeness better than CL only, and CL in upright position may be considered as a functional test. In two third of the women with a CL ≤30mm or BS >5, labour indeed started within 96 hours. The rather low predictive values (sensitivity 83% and 49%; specificity 41% and 80%; PPV 65% and 78%; and NPV 65% and 51%, respectively) may be explained by the large variation in CL and CL changes preceding spontaneous onset of labour, as described in *chapter 5*. In conclusion, women with short cervix on TVS or favourable Bishop Score beyond 41 weeks of gestation have a high chance of spontaneous onset of labour within 96 hours. It is conceivable that the decision for induction of labour is postponed for these women. On the other hand, a CL >30mm or Bishop Score <5 is not informative.

In *chapter 8* we aimed to predict the mode of delivery in women with a previous CS by TVS of the cervix at weekly interval from 36 weeks of gestation onwards. We included women

with a previous CS for failure of progress and women with a previous elective CS for breech presentation. The latter group may resemble nulliparous women, whereas the first group may be considered parous women. Women with a previous CS for failure of progress were most likely to deliver by repeat CS after 41 weeks of gestation. We observed a success rate of 80% after trial of labour, which is in accordance with previous literature[49]. TVS was not predictive for the mode of delivery, however this may be due to the limited number of patients (n=36) that could be included. A single CL measurement at 37 weeks of gestation was predictive of spontaneous onset of labour before 41 weeks of gestation, but only in the group with a previous CS for breech presentation. These results are concordant with our longitudinal study in nulliparous women (*chapter 5*).

Conclusions and recommendations for clinical use

1. TVS is the gold standard for CL measurements. CL should be measured in a straight line from the internal to the external os, with an empty bladder and without pressure on the cervix by the ultrasound probe.
2. Dynamic changes of the cervix may be present at early gestation and long before spontaneous onset of labour.
3. Transperineal sonography is a reliable substitute for TVS of the cervix at term. Disadvantages are the need for an experienced investigator, the high percentage of failure to obtain a clear image and the (slight) discomfort for the patient.
4. There is considerable variation in CL and CL changes preceding spontaneous onset of labour in nulliparous women. The ranges of physiology are large.
5. At 37 weeks of gestation, a single CL measurement predicts spontaneous onset of labour in both nulliparous women and women with a previous CS for breech presentation.
6. At prolonged pregnancy, both CL and the Bishop Score predict spontaneous onset of labour within 96 hours from ultrasound or digital examination.
7. Unlike the preterm period of pregnancy, when CL measurements have a high NPV and low PPV for the prediction of spontaneous onset of labour, the PPV of a short cervix at term is high, but with low sensitivity and NPV.
8. The mode of delivery at term is best predicted by CL in upright position, and this may be considered a functional test of engagement of the fetal occiput and subsequent CL changes.
9. The Bishop Score may reflect cervical ripeness better than a single CL measurement, since it consists of assessment of five different aspects of the cervix.
10. The intra-individual variation in CL and large variation in CL changes preceding spontaneous onset of labour hamper the clinical use of CL measurements at term.

When CL measurements are used in clinical practice, it is necessary to understand physiology of the cervix at term. Unfortunately, we found large variation in CL changes preceding spontaneous onset of labour, which restricts clinical utilization. However, a few recommendations can be made. CL has wide normal ranges throughout pregnancy. Before term, a short cervix is exceptional, however the chance of delivering in case of a short cervix is comparable to the flip of a coin. In contrast, preterm delivery is highly unlikely in case of a long cervix. At term, it is exactly the opposite. A long cervix at term is exceptional, although it does not at all exclude spontaneous onset of labour within short time. A short cervix at 37 weeks is reassuring, however spontaneous onset of labour may not be due until weeks. A short cervix on TVS at prolonged pregnancy may be in favour of expectant management. On the other hand, a short cervix at pre-induction TVS increases the chance of a vaginal delivery. Adding a maternal postural change to the examination improves the assessment of the functional status of the cervix. With knowledge of its limitations, TVS of the cervix can be used at term gestation.

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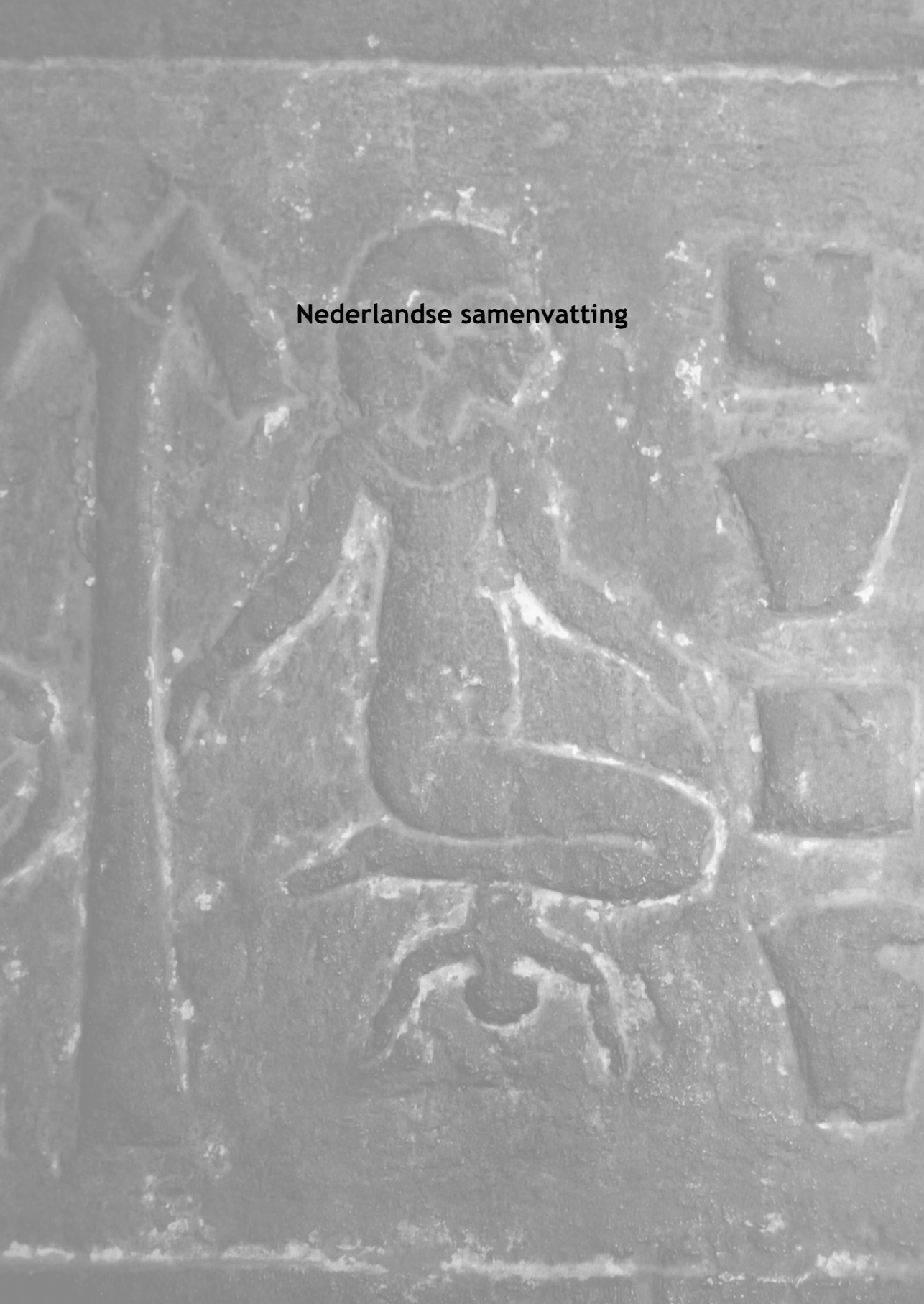

Nederlandse samenvatting

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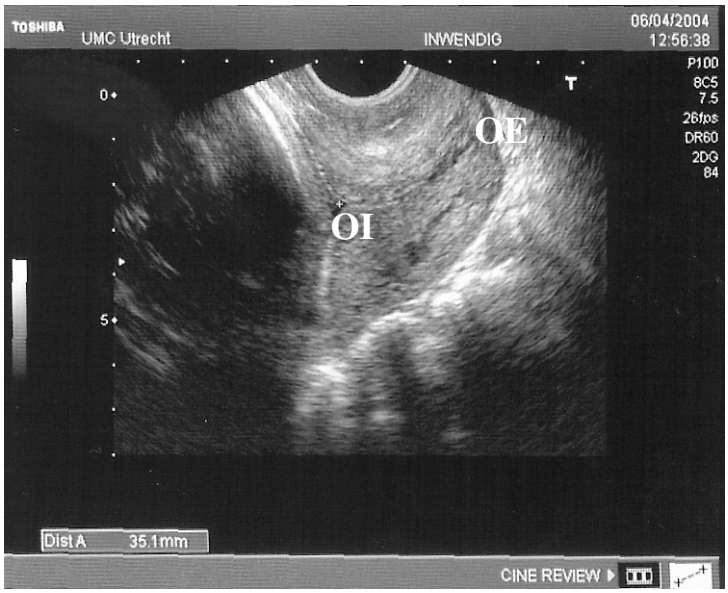
Gedurende de zwangerschap wordt de baarmoedermond (cervix) getransformeerd van een stugge, kraakbeen-achtige structuur tot een weke, zachte structuur. Dit "rijp" worden van de cervix is nodig om aan het einde van de zwangerschap het ontsluiten en daarmee de geboorte mogelijk te maken[1].
De rijpheid van de cervix wordt vanaf 1960 ingeschat door middel van de Bishop Score[2]. Dit is een score die gebaseerd is op vijf aspecten van de cervix: ontsluiting, verstrijking, weekheid en positie van de cervix en de indaling van het voorliggend deel van de foetus. Deze score wordt gebruikt om de rijpheid van de cervix voorafgaand aan een inleiding in te schatten, maar ook om te vroege rijping te beoordelen bij een dreigende vroeggeboorte.
Vanaf de tachtiger jaren wordt voor deze indicaties de vaginale echoscopie van de cervix gebruikt. Een voordeel van de vaginale echoscopie is dat uitrijping van de cervix in een vroeg stadium gezien kan worden. Het eerste teken van rijpen van de cervix is namelijk het openen van het ostium internum (OI; figuur 1), dat bij een gesloten ostium externum (OE; figuur 1) niet gevoeld kan worden via de vagina. Bovendien is de vaginale echo gemakkelijk aan te leren, zelfs voor onervaren onderzoekers[3] en is de techniek goed reproduceerbaar[4-6].



Figuur 1: Vaginale echo van de cervix

Voor het voorspellen van een vroeggeboorte bij vrouwen met weeënactiviteit vóór de uitgerekende periode heeft de cervixlengte (CL) meting een hoge negatief voorspellende waarde[7;8]. De positief voorspellende waarde is daarentegen helaas niet hoger dan 50%. Dat wil zeggen: als de CL lang is dan is de kans op vroeggeboorte uiterst klein (1-2%); is de CL

echter kort, dan bedraagt de kans op een bevalling binnen 7 dagen 40 tot 47%. Ook voor screening naar de kans op vroeggeboorte in een algemene populatie is de CL meting alleen nuttig om vrouwen met een laag risico te identificeren[9]. De optimale afkapwaarde voor een korte cervix varieert sterk tussen de verschillende studie groepen.
Het is opvallend dat bij de introductie van de CL meting in de klinische praktijk, geen grote onderzoeken verricht zijn naar de veranderingen van de cervix voorafgaand aan de baring in de uitgerekende periode. Dit promotie onderzoek is opgezet om meer kennis te verkrijgen van de fysiologische veranderingen voorafgaand aan spontane weeënactiviteit in de uitgerekende periode en om deze mogelijke veranderingen te relateren aan de kans op het optreden van een spontane vaginale bevalling, cq de noodzaak de bevalling in te leiden. Kennis over de fysiologie van de cervix is nodig om pathologische veranderingen te kunnen interpreteren.

Het doel was om een antwoord te verkrijgen op de volgende vragen:

1-Wat is de "gouden standaard" om optimale CL metingen te verkrijgen, wat zijn de valkuilen en wat is de relevantie van de verschillende metingen die verricht kunnen worden aan de cervix?
2-Hoeveel fluctueert de CL en wat veroorzaakt deze fluctuaties?
3-Hoe betrouwbaar zijn transperineale CL metingen in de uitgerekende periode?
4-Verandert de cervix voorafgaand aan spontane weeënactiviteit in de uitgerekende periode en kan het moment van weeënactiviteit voorspeld worden aan de hand van CL metingen of door veranderingen in CL in de tijd?
5-Kunnen CL metingen, gemeten in liggende of staande positie van de zwangere voorafgaand aan een inleiding van de baring, beter de kans op een vaginale bevalling voorspellen dan de Bishop Score?
6-Kunnen de vaginale echo van de cervix en de Bishop Score het alsnog optreden van spontane weeënactiviteit na 41 weken zwangerschapsduur voorspellen?
7-Kunnen vrouwen met een verhoogd risico op een tweede keizersnede worden geïdentificeerd door seriële metingen van de cervix?

In *hoofdstuk 2* hebben we verschillende technieken van echoscopie van de cervix en de factoren die beeldvorming van de cervix beïnvloeden onderzocht door een overzicht te maken van de bestaande literatuur. Er zijn drie verschillende echoscopische benaderingen mogelijk om de cervix zichtbaar te maken, namelijk transabdominaal, transperineaal and transvaginaal. Een nadeel van de transabdominale benadering is dat een volle blaas noodzakelijk is om de cervix goed a vue te krijgen[10]. Het is echter aangetoond dat een volle blaas de cervix artificieel kan verlengen[11;12]. Bovendien is identificatie van de oriëntatiepunten van de cervix, namelijk het ostium internum en externum en het cervicale kanaal, vaak moeilijk in geval van een korte cervix[10]. De transperineale benadering heeft als nadeel dat schaduw van darmgassen

of van de symfyse beeldvorming van de cervix kunnen vertroebelen[13]. Het oplichten van de heupen van de zwangere kan de beeldvorming wellicht verbeteren, maar het percentage waarin beeldvorming van de cervix onmogelijk is kan oplopen tot 12% van de gevallen. Dit percentage is afhankelijk van de ervaring van de onderzoeker[14-20]. Transvaginale echoscopie van de cervix moet beschouwd worden als de gouden standaard. Beeldvorming is mogelijk in bijna 100% van alle gevallen en de techniek is gemakkelijk te leren, ook voor onervaren onderzoekers[3]. De methode is goed reproduceerbaar[4-6], als metingen verricht worden met een lege blaas en druk op de cervix door de transducer voorkomen wordt. Als de cervix gebogen is, moet de CL gemeten worden in een rechte lijn van het ostium internum naar het ostium externum[3]. Funneling kan aanwezig zijn en is waarschijnlijk fysiologisch in het derde trimester van de zwangerschap[21;22]. Rond de 20 weken zwangerschapsduur verhoogt de aanwezigheid van een funnel het risico op een vroeggeboorte zowel voor vrouwen met een hoog risico[23-25] (OR 5.61; 95% CI 4.40;10.58) als voor vrouwen met een laag risico[26;27] op vroeggeboorte (OR 9.44; 95% CI 8.30;10.58). De vorm van de funnel verandert vaak tijdens het echo-onderzoek. Het vastleggen van afmetingen van de funnel suggereert daarmee ten onrechte nauwkeurigheid[28]. Als de cervix alleen gemeten wordt in liggende positie, dan kan de aanwezigheid van een funnel verborgen blijven[28-32]. Provocatietesten zoals druk op de fundus uteri en het herhalen van de vaginale echo in staande positie moeten worden verricht als funneling niet zichtbaar is bij vrouwen met een verhoogd risico op vroeggeboorte, om te voorkomen dat de juiste diagnose gemist wordt.

Spontane veranderingen van de cervix over een korte observatie periode, zijn al eerder beschreven[25;28;32]. In *hoofdstuk 3* hebben we onderzocht welke factoren de beeldvorming van de cervix beïnvloeden, door continue echoscopische opnames van de cervix te maken gedurende 30 minuten bij 6 nulliparae en 12 parae, die evenredig verdeeld waren in hoog en laag risico voor vroeggeboorte. Het onderzoek werd eenmalig verricht tussen de 23 en 40 weken zwangerschapsduur. Eén vrouw beviel bij 34 weken zwangerschapduur, alle anderen na de 36e week. Het gemiddelde verschil tussen de kortst en langst gemeten CL gedurende het onderzoek bedroeg 10.9mm (spreiding 1.6-22.0mm). Sommige vrouwen vertoonden veranderingen in de lengte van de cervix die geassocieerd waren met foetale bewegingen en darmperistaltiek. Wij hebben met dit onderzoek aangetoond dat dynamische veranderingen van de cervix al vroeg in de zwangerschap aanwezig kunnen zijn en reeds lang voordat spontane weeënactiviteit begint. Beperkingen van het onderzoek zijn de kleine studiepopulatie en de grote variatie in zwangerschapsduur ten tijde van het echo-onderzoek. De voorspellende waarde van deze dynamische veranderingen voor het optreden van spontane weeënactiviteit kan met dit onderzoek dan ook niet vastgesteld worden. Het feit dat er een grote variatie in CL bestaat, impliceert dat beslissingen in de klinische praktijk niet gebaseerd moeten worden op één enkele Cl meting. Herhaalde metingen van de CL geven weliswaar informatie over de variatie in CL, maar de klinische relevantie

hiervan is nog niet aangetoond.
Transperineale echoscopie van de cervix lijkt een bruikbaar alternatief te zijn voor transvaginale echo van de cervix vòòr 37 weken zwangerschapsduur, indien uitgevoerd door een ervaren onderzoeker[14-20]. In *hoofdstuk 4* hebben we de betrouwbaarheid en acceptatie van deze methode onderzocht in het derde trimester van de zwangerschap en vergeleken met de periode rond 20 weken zwangerschapsduur. Transperineaal gemeten CL correleerde goed met transvaginaal gemeten CL in het derde trimester van de zwangerschap (Pearson correlatie 0.79; 95% CI 0.63;0.88) en zelfs nog beter bij metingen rond 20 weken (Pearson correlatie 0.94; 95% CI 0.82;0.98). Echter, in respectievelijk 19% en 30% van de gevallen was het niet mogelijk om duidelijke beeldvorming van de cervix te verkrijgen door schaduwvorming en beperkte ervaring van onze onderzoekers met de techniek. Het is eerder beschreven dat, door ervaring op te doen met de transperineale methode, het percentage niet optimale beeldvorming van de cervix gereduceerd kan worden van 55% tot 12%[16]. De transvaginale beelden van de cervix werden door onze onderzoekers beter gewaardeerd dan de transperineale beelden, vooral rond de 20 weken zwangerschapsduur. In het derde trimester was identificatie van de oriëntatiepunten van de cervix gemakkelijker door het ingedaalde hoofd van de foetus. De meeste zwangeren (68%) ervaarden de transperineale methode niet of nauwelijks pijnlijk, maar wel pijnlijker dan de transvaginale methode (Wilcoxon signed rank test; P=0.01). Wij concludeerden dat transperineale echoscopie van de cervix een bruikbaar alternatief kan zijn voor de transvaginale echo in het derde trimester van de zwangerschap, maar alleen in de handen van een ervaren onderzoeker. Beeldvorming van de cervix met de oriëntatiepunten lijkt gemakkelijker met het vorderen van de zwangerschap door indaling van het foetale hoofd.

Het doel van *hoofdstuk 5* was inzicht te verkrijgen in fysiologische veranderingen van de cervix voorafgaand aan spontane weeënactiviteit in de uitgerekende periode van de zwangerschap. Hiertoe verrichtten wij wekelijkse seriële CL metingen bij 162 nulliparae vanaf 36 weken zwangerschapsduur. Transvaginale echoscopie van de cervix werd verricht in liggende en staande positie. De liggende en staande metingen correleerden goed (Pearson correlatie 0.90; 95% CI 0.84;0.94). De laatste CL meting voorafgaand aan spontane weeënactiviteit correleerde significant met het echo-bevallings interval, hoewel de correlatie coëfficient laag was (spreiding 0-12 dagen; Pearson correlatie -0.26; 95% CI -0.45;-0.05). Bij 31% van de vrouwen bedroeg de laatste CL, gemeten kort voor de bevalling nog meer dan 30mm. De seriële metingen toonden dat bij de helft van de populatie de CL afnam in de laatste weken voorafgaand aan de bevalling, d.w.z. geleidelijk over een periode van meer dan twee weken, of vrij abrupt tijdens de laatste twee weken. Dit was in twee kleine onderzoeken eerder beschreven[21;22]. In de andere helft van onze populatie zagen wij echter geen verandering in CL tot vlak –maximum 7 dagen– voorafgaand aan de bevalling. Eén enkele meting bij 37 weken zwangerschapsduur, zowel liggend als stand, was voorspellend voor het optreden van spontane weeënactiviteit vóór 41 weken zwangerschapsduur, echter met lage sensitiviteit

en negatief voorspellende waarde (liggend en staand: sensitiviteit 46% en 53%; specificiteit 78% en 72%; PVW 82% en 81%; en NVW 40% en 40%). Concluderend was er sprake van grote inter-individuele variatie in CL en in veranderingen van de cervix voorafgaand aan spontane weeënactiviteit. Dit beïnvloedt de voorspellende waarde voor het optreden van spontane weeënactiviteit en moet in overweging genomen worden bij de interpretatie van één of herhaalde CL metingen.

Nulliparae hebben een hogere kans op een langdurige bevalling na een inleiding van de bevalling en een hoger risico op een keizersnede[33;34]. De voorspellende waarde van een CL meting of van de Bishop Score voorafgaand aan een inleiding is al eerder onderzocht. Onderlinge vergelijking van deze onderzoeken is moeilijk vanwege het gebruik van verschillende uitkomstmaten en methoden van inleiden van de bevalling. In *hoofdstuk 6* onderzochten we de voorspellende waarde van de CL meting, zowel liggend als staand gemeten, en van de Bishop Score aan het begin van de inleiding in de uitgerekende periode van de zwangerschap voor de kans op een vaginale bevalling. De CL meting in staande positie was de enige significante voorspeller voor een vaginale bevalling na een inleiding (OR 1.14; 95% CI 1.02-1.27). De CL metingen in zowel liggende en staande positie waren betere voorspellers van het risico op een keizersnede dan de Bishop Score. De Bishop Score was de beste voorspeller van de duur van de bevalling. In eerdere studies was de CL meting ook de beste voorspeller van een vaginale bevalling na een inleiding, maar met een lage sensitiviteit en negatief voorspellende waarde[35-42]. Wanneer een geslaagde inleiding gedefinieerd wordt als een vaginale bevalling binnen 24 uur, dan lijkt de Bishop Score even goed in het voorspellen van een geslaagde inleiding als de echoscopisch gemeten CL[43-47]. Dit kan verklaard worden door het feit dat met de Bishop Score vijf verschillende aspecten van de cervix worden beoordeeld en dit wellicht een betere indruk geeft van de rijpheid van de cervix dan alleen CL. CL in staande positie zou kunnen worden beschouwd als een functionele test van de cervix, die indaling van het foetale hoofd en daarmee optredende veranderingen in CL beoordeelt. Wellicht wordt een disproportie op deze manier ontdekt, en verklaart dit het feit dat de CL in staande positie de beste voorspeller was voor een vaginale bevalling.

Er is consensus dat zwangeren die meer dan 41 weken zwanger zijn geïnformeerd moeten worden over de risico's en voordelen van afwachtend beleid in vergelijking met het inleiden van de baring. Vooral bij nulliparae, die een verhoogde kans op een langdurige bevalling[48] en een keizersnede[34;41;49] hebben na het inleiden van de baring, is het nuttig om vast te stellen wie alsnog een grote kans heeft op het eerdaags spontaan in partu komen, om daarmee onnodige inleidingen te voorkomen. In *hoofdstuk 7* onderzochten wij de voorspellende waarde van de CL meting en de Bishop Score bij 85 nulliparae met een zwangerschapsduur van meer dan 41 weken, voor het optreden van spontane weeënactiviteit. Spontane

weeënactiviteit binnen 96 uur kon worden voorspeld in geval van een Bishop Score >5 en een CL ≤30mm (respectievelijk: OR 1.46; 95% CI 1.07;1.98; en OR 0.92; 95% CI 0.87;0.98). Deze resultaten zijn in overeenstemming met één eerder vergelijkbaar onderzoek[50]. Verandering van positie van de zwangere verbeterde de voorspellende waarde van de CL meting voor het optreden van spontane weeënactiviteit niet, maar de CL meting in staande positie was wel de enige significante voorspeller voor het risico op een keizersnede (OR 1.07; 95% CI 1.01;1.12). Zoals besproken in het vorige hoofdstuk kan dit wellicht verklaard worden door het feit dat de CL meting in staande positie beschouwd kan worden als een functionele test van de cervix. Bij tweederde van de vrouwen met een CL ≤30mm of een Bishop Score >5 begon de spontane weeënactiviteit inderdaad binnen 96 uur. De lage voorspellende waarde (sensitiviteit 83% en 49%; specificiteit 41% en 80%; PVW 65% en 78%; en NVW 65% and 51%) kan verklaard worden door de grote variatie in CL en veranderingen in CL voorafgaand aan spontane weeënactiviteit zoals beschreven is in *hoofdstuk 5*. Concluderend hebben vrouwen met een korte cervix bij transvaginale echo of een gunstige Bishop Score na 41 weken zwangerschapsduur een hoge kans op spontane weeënactiviteit binnen 96 uur. Het is denkbaar dat bij deze vrouwen de beslissing tot inleiden wordt uitgesteld. Een CL >30mm of Bishop Score <5 geeft daarentegen weinig extra informatie.

Doel van *hoofdstuk 8* was bij vrouwen met een keizersnede in de voorgeschiedenis de manier van bevallen voorspellen door seriële CL metingen vanaf 36 weken zwangerschapsduur. Alleen vrouwen met een keizersnede vanwege niet vorderende baring en vanwege een stuitligging werden geïncludeerd. De laatste groep kan als nulliparae beschouwd worden, terwijl de eerste groep waarschijnlijk het meest lijkt op parae. Vrouwen met een keizersnede in de voorgeschiedenis vanwege een niet vorderende baring hadden de grootste kans op een tweede keizersnede na 41 weken zwangerschapsduur. Na 'trial of labour' beviel 80% vaginaal, wat overeen komt met eerdere literatuur[51]. De wijze van bevallen kon niet worden voorspeld door transvaginale echo van de cervix, maar dit kan wellicht verklaard worden door de kleine populatie (n=36) die geïncludeerd kon worden. Spontane weeënactiviteit voor 41 weken zwangerschapsduur kon voorspeld worden door één enkele CL meting bij 37 weken zwangerschapsduur bij vrouwen met een keizersnede in de voorgeschiedenis vanwege een stuitligging. Deze resultaten komen overeen met die van ons longitudinale onderzoek bij nulliparae (*hoofdstuk 5*).

Conclusie en aanbevelingen

1. Transvaginale echoscopie is de gouden standaard voor CL metingen. CL metingen moeten worden verricht met een lege blaas en druk op de cervix door de transducer moet worden vermeden. De cervix moet worden gemeten in een rechte lijn van het ostium internum tot het ostium externum.
2. Dynamische veranderingen van de cervix kunnen al vroeg in de zwangerschap aanwezig zijn en lang voordat de baring begint.
3. Transperineale echoscopie van de cervix is een betrouwbaar alternatief voor transvaginale echoscopie in het derde trimester van de zwangerschap. Nadelen zijn het hoge percentage waarin geen beeldvorming van de cervix kan worden verkregen, de afhankelijkheid van de ervaring van de onderzoeker, en het (lichte) ongemak voor de patiënt.
4. Bij nulliparae is er, voorafgaand aan spontane weeënactiviteit in de uitgerekende periode een grote variatie in CL en veranderingen in CL in de tijd. De fysiologie verschilt sterk tussen individuen.
5. Eén enkele CL meting bij 37 weken zwangerschapsduur voorspelt spontane weeënactiviteit voor 41 weken zwangerschapsduur bij nulliparae en bij vrouwen met een keizersnede in de voorgeschiedenis vanwege stuitligging.
6. Echoscopische CL meting en Bishop Score voorspellen spontane weeënactiviteit binnen 96 uur bij nulliparae met een zwangerschapsduur van meer dan 41 weken.
7. In de uitgerekende periode van de zwangerschap heeft een CL meting een hoge positief voorspellende waarde (PVW) voor het optreden van spontane weeënactiviteit, en een lage sensitiviteit en negatief voorspellende waarde (NVW). Dit is tegengesteld aan de periode vóór 37 weken waarin de NVW van de CL meting hoog is en de PVW laag.
8. De wijze van bevallen wordt het beste voorspeld door een CL meting in staande positie in de uitgerekende periode van de zwangerschap. Deze meting lijkt een functionele test van cervix en baringskanaal die indaling van de foetale hoofd inschat.
9. De vijf aspecten van de Bishop Score samen geven de rijpheid van de cervix beter weer dan alleen een CL meting.
10. De intra-individuele variatie in CL en grote variatie in CL veranderingen voorafgaand aan spontane weeënactiviteit beperken de klinische toepasbaarheid van de CL meting in de uitgerekende periode van de zwangerschap.

Bij gebruik van CL metingen in de klinische praktijk is het essentieel om de fysiologie van de cervix in de uitgerekende periode te begrijpen. Helaas vonden wij een grote variatie in veranderingen in CL die voorafgaan aan spontane weeënactiviteit. Dit beperkt de klinische

toepasbaarheid. Toch kunnen enkele aanbevelingen worden gedaan. De normaalwaarden voor CL gedurende de zwangerschap zijn breed. Vóór de uitgerekende periode is een korte cervix uitzonderlijk, maar is de kans op een vroeggeboorte bij een korte cervix vergelijkbaar met het opgooien van een munt. Als de cervix daarentegen lang is, dan is een dreigende vroeggeboorte hoogst onwaarschijnlijk. In de uitgerekende periode is het net omgekeerd. Een lange cervix is uitzonderlijk, hoewel dit geenszins spontane weeënactiviteit op korte termijn uitsluit. Een korte cervix bij 37 weken zwangerschap is geruststellend, maar het begin van de baring kan nog weken op zich laten wachten. Voorbij 41 weken zwangerschapsduur kan een korte cervix pleiten voor afwachtend beleid. Aan de andere kant verhoogt een korte cervix ook de kans op een vaginale bevalling na een inleiding. Het toevoegen van de CL meting in staande positie aan het onderzoek lijkt inzicht in de functionaliteit van de cervix en eventuele disproportie tussen hoofd en baringskanaal te verhogen. Als men zich bewust is van de beperkingen van het onderzoek, dan kan de echoscopische CL meting in de uitgerekende periode klinisch toegepast worden.

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List of abbreviations

AFI	Amnion Fluid Index
BMI	Body mass index
BS	Bishop Score
CL	Cervical length
CS	Caesarean section
CI	Confidence interval
GA	Gestational age
HR	Hazard ratio
NPV	Negative predictive value
OR	Odds ratio
PD	Preterm delivery
PGE2	Prostaglandin E2
PPV	Positive predictive value
PROM	Premature rupture of membranes
TOL	Trial of labour
TP	Transperineal
TV	Transvaginal
TVS	Transvaginal sonography
US	Ultrasound
VBAC	Vaginal birth after caesarean section

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Madelon is getrouwd met Sander Meijer en samen hebben zij een dochter Eva.

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