

Comparison of transvaginal sonography in recumbent and standing maternal positions to predict spontaneous preterm birth in singleton and twin pregnancies

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KEYWORDS: cervical insufficiency; cervical shortening; funneling; transvaginal ultrasound

ABSTRACT

Objective To evaluate whether serial transvaginal sonographic examination of the cervix with the woman in a standing position improves the prediction of spontaneous preterm birth (SPB) compared with the conventional posture.

Methods For both a recumbent and upright maternal position, the inter- and intraobserver agreement of cervical length (CL) measurement was calculated. In 363 pregnancies at risk for SPB, we determined prospectively CL and funnel width (FW) including differences between the positions and between longitudinal measurements from 15 weeks onwards. Multivariate logistic regression analysis, contingency tables and receiver–operating characteristics (ROC) curves were used. Data were stratified according to singleton or twin pregnancy, maternal position, gestational age at examination and different cut-off values to predict SPB < 36 weeks.

Results The interobserver variability in each position was similar, with an interclass correlation coefficient (95% CI) of 0.952 (0.811–0.984) in the recumbent and 0.942 (0.837–0.978) in the upright maternal position. After exclusion of pregnancies with iatrogenic preterm birth, 15/138 (11%) singletons and 29/153 (19%) twin pairs were born at < 36 weeks. The incidence of funneling was greater in an upright compared with a recumbent maternal position by 12.3% in singleton and 13.1% in twin pregnancies before 25 weeks, and by 13.0% and 21.6% between 25 and 30 weeks, respectively. This resulted in an earlier and more accurate prediction of SPB by transvaginal ultrasound in an upright compared with a recumbent maternal position, which could be shown by all applied statistical methods. The influence of posture on the prognostic value of the CL varied depending on the cut-off value. Differences in CL or FW between 15–20 and

25–30 weeks predicted SPB better than did differences between shorter intervals.

Conclusions Evaluation of the cervix with the woman in the upright position permits earlier detection of funneling. This may enable earlier and more appropriate intervention to avoid SPB. Copyright © 2006 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

The uterine cervix is a dynamic anatomical structure. Its mechanical properties, changing from firm and rigid to soft and elastic, depend mainly on the regulation of connective tissue and its extracellular matrix by an inflammatory-like mechanism. Ideally, the cervix dilates gradually towards term and during delivery¹; in spontaneous preterm birth (SPB), it opens prematurely; in cervical dystocia, it fails to dilate adequately.

The cervix consists predominantly of fibrous connective tissue with 80% of the total protein content formed by collagen and 10–15% being smooth muscle fibers². Cervical ripening is characterized by a high collagen solubility and collagenolytic activity, a decrease in total collagen content and an influx of inflammatory cells with increasing levels of cytokines and prostaglandins³. During dilatation, digestion of denatured collagen leads to further loss of collagen and, consequently, of firmness⁴. Local or ascending intrauterine infections are thought to lead to activation of all the components of the preterm labor syndrome, whereby functional loss of cervical integrity is the common terminal pathway⁵. Conversely, cervical shortening and opening of the internal os may facilitate the ascension of microorganisms, injuries to the decidua–chorioamnion interface and, finally, membrane activation and amnionitis⁵.

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In singleton pregnancies with SPB, a positive microbial culture retrieved by amniocentesis was observed in 21.6% of cases⁶. In contrast, microbial invasion of the amniotic cavity occurred in only 11.9% of twin gestations presenting with SPB⁷. Although new results have shown that subclinical endometrial infection and inflammation can be a causal factor for SPB⁸, intra-amniotic infection does not seem to be the only reason responsible for a percentage of SPBs in singleton pregnancies nor for the excessive rate of SPB in twin pregnancies. Uterine overdistension and the fact that the cervix is aligned centrally with no support except for the non-resistant vagina may be another pathogenetic factor involved mainly in multiple gestations.

Transvaginal sonography (TVS) has been used to examine the cervix for approximately 15 years⁹. It is recognized that a short cervix detected by TVS with the woman in a recumbent position is a strong predictor of SPB for both singleton and twin pregnancies, and the predictive value depends on the gestational age at detection, the cut-off value and even additional clinical symptoms¹⁰. To examine specifically mechanical properties of a cervix at risk for SPB, transfundal pressure and straining have been proposed^{11,12}. Serial changes in cervical length (CL) and funnel width (FW) have been established for both recumbent and upright maternal positions; the differences between the positions in both CL and FW were higher at late compared with early gestation and in twin compared with singleton pregnancies of the same gestational age^{13,14}. The observation that the structure of the cervix may change dynamically in an upright position in a few patients showing a dilated internal os, increasing prolapse of the fetal membranes and sometimes even membrane dissociation, was the stimulus to perform TVS in both positions in all our at-risk patients.

The aim of this study was to determine if serial transvaginal examinations of the cervix with the mother in the upright position improves the prediction of SPB compared with examination of the cervix with the mother in the conventional recumbent posture.

METHODS

TVS was performed with an ATL 5000 HDI (Philips, Enthoven, The Netherlands,) ultrasound machine equipped with a 8.5-MHz transvaginal probe. Before each examination, the woman was asked to empty her bladder. Recognition of the lowermost edge of the maternal urinary bladder was used to detect the upper limit of the uterine cervix. The sonographic image was followed in a sagittal view until the endocervical canal and the cervical gland area were visualized. Compression of the cervix was avoided. The length of the closed portion of the endocervical canal was measured in a position whereby the anterior and posterior cervix appeared to be equally thick. Funneling was defined as any opening of the internal os with protrusion of the membranes into the cervical canal (Y-, V- or U-shaped) as opposed to a perpendicular

T-shaped relationship between the cervix and the fetal membranes ('no funneling'). FW was measured at the level of the suspected former internal os. Every examination was performed with the woman in a supine and an upright position. For the latter, the patient was asked to place one foot on a footstool and to guide the transducer herself into the lower part of the vagina until it could be directed by the examiner. Thereby both the physician and the patient could observe whether postural stress affected the cervix. Before a result was interpreted, the woman stood or lay in position for at least 1 min.

The inter- and intraobserver agreement in determining the CL between two observers with different expertise in TVS (Observer 1 (B.A.): 15 years; Observer 2 (C.R.): 15 days) was assessed in 10 singleton and 10 twin pregnancies. In all patients, 10 consecutive measurements were performed alternatively by each of the examiners with the woman in the recumbent and standing positions. The observers were blinded to the results during the examination. The intra- and interclass correlation coefficient (CC) and Cronbach's alpha reliability coefficient (RC) with 95% CI were calculated. Patients were recruited from our outpatient clinic at a gestational age of 15–30 weeks. In these patients, an opening of the internal os occurred too rarely to determine the intra- or interobserver agreement for measurement of FW.

To detect the predictive value of TVS in different positions and at different gestational ages data were collected prospectively between 2001 and 2004 from 186 twin and 177 singleton pregnancies at increased risk for SPB (history of SPB, uterine abnormality and early symptoms of SPB such as blood loss or preterm contractions). The patients were recruited from our outpatient clinic and were included from 15 weeks onwards. All measurements were performed by the same examiner (Observer 1). After delivery, we excluded data from patients with iatrogenic preterm birth (< 36 weeks) and from pregnancies in which the dataset did not include at least three consecutive measurements within different gestational age-groups (I: 15 to 19 + 6 weeks; II: 20 to 24 + 6 weeks, III: 25 to 29 + 6 weeks).

The primary outcome of the study was spontaneous preterm delivery < 36 weeks. For cases in which more than one measurement was performed within one gestational age-group (i.e. with an interval of less than 5 weeks), only the earliest measurement within this age-group was considered.

McNemar's test was used to calculate significant differences in FW and CL between positions. Stepwise forward multiple logistic regression analysis was conducted for CL and FW in both positions, in order to test whether they were related to a reduced (increasing values of CL) or an increased (increasing values of FW) risk for SPB at < 36 weeks. All parameters were analyzed as continuous variables. In addition, differences between gestational age-groups I and II, II and III, and I and III were analyzed.

Contingency tables were established in order to calculate sensitivity, specificity, positive and negative

Table 1 Intra- and interobserver correlation coefficients (CC) and Cronbach's alpha reliability coefficients (α -RC)

Pregnancy type	CL	Intraobserver				Interobserver	
		Observer 1		Observer 2		CC (95% CI)	α -RC
		CC (95% CI)	α -RC	CC (95% CI)	α -RC		
Singleton	re	0.990 (0.978–0.997)	0.990	0.979 (0.951–0.994)	0.982	0.930 (0.706–0.983)	0.941
	st	0.981 (0.956–0.994)	0.982	0.981 (0.957–0.994)	0.982	0.930 (0.706–0.983)	0.940
Twin	re	0.993 (0.985–0.998)	0.993	0.991 (0.979–0.997)	0.991	0.963 (0.776–0.992)	0.975
	st	0.995 (0.988–0.998)	0.995	0.987 (0.971–0.996)	0.986	0.963 (0.766–0.992)	0.957
Total	re	0.990 (0.982–0.995)	0.991	0.990 (0.982–0.995)	0.990	0.952 (0.811–0.984)	0.966
	st	0.991 (0.984–0.996)	0.992	0.984 (0.971–0.993)	0.984	0.942 (0.837–0.978)	0.951

CL, cervical length; re, recumbent; st, standing.

predictive values (PPV and NPV), positive and negative likelihood ratios (LR) and the diagnostic odds ratio (DOR; ratio of positive LR to negative LR) to determine the risk of SPB at < 36 weeks. The DOR was used to discriminate the power of a test. In the case of 'zero entries', the DOR was calculated by adding 0.5 to all cells of the contingency tables¹⁵. Receiver–operating characteristics (ROC) curves were calculated for several cut-off values of CL and FW to predict SPB at < 36 weeks. The Statistical Package for Social Sciences (version 12.0, SPSS, Chicago, IL, USA) was used for all evaluations.

RESULTS

There was excellent intra- and interobserver agreement for CL measurements obtained by both investigators for both recumbent and upright maternal positions in both singleton and twin pregnancies (Table 1).

After exclusions, the main study population consisted of 138 singleton pregnancies at risk for SPB (Table 2) and 153 twin pregnancies. The mean maternal age was 32 years for singleton and 31 years for twin pregnancies. The mean gestational age at delivery was 38 (range, 24.1–42.2) weeks for singletons and 36 (range, 26.4–40.0) weeks for twin pairs, and their respective rates of SPB at < 36 weeks were 15/138 (10.9%) and 29/153 (19%) (Table 2).

The incidence of funneling in the upright compared with the recumbent maternal position was greater by 12.3% in singleton and by 13.1% in twin pregnancies between 20 and 25 weeks, and by 13.0% and 21.6%, respectively, between 25 and 30 weeks (Table 3).

Table 2 Characteristics of the study population: 138 singleton pregnancies at risk of spontaneous preterm birth (SPB) and 153 twin pregnancies

Characteristic	Singleton pregnancies (n = 138)	Twin pregnancies (n = 153)
Maternal age (years, mean (range))	32 (23–42)	31 (16–40)
Gravida I (n (%))	14 (10.1)	73 (48.0)
History of SPB* (< 36 weeks) (n (%))	66 (47.8)	13 (8.5)
Ovulation stimulation (n (%))	1 (0.7)	9 (5.9)
IVF/ICSI (n (%))	5 (3.7)	49 (32.0)
Spontaneous delivery < 36 weeks (n (%))	15 (10.9)	29 (19.0)
Birth weight (g, mean (range))		
Child 1	3008 (850–4500)	2443 (650–3720)
Child 2		2416 (1060–3780)

*Only valid for multigravid pregnancies. ICSI, intracytoplasmic sperm injection; IVF, *in-vitro* fertilization.

Results of the stepwise forward multiple logistic regression analysis are shown in Table 4. We only show results obtained between 20 and 25 weeks (Group II), including differences between measurements of Groups I and II, since this period is most frequently used for risk estimation of SPB. When absolute measurements of FW or CL were integrated in the regression model, a long cervix decreased and a wide FW increased the risk of SPB. The results were only significant in the upright position (Table 4). When comparing differences of FW and CL between both positions, only Δ FW and not Δ CL

Table 3 Proportion of patients with funneling in the recumbent and standing positions

Gestational age (weeks)	Proportion of funneling (n (%)) in singleton pregnancies (n = 138)			Proportion of funneling (n (%)) in twin pregnancies (n = 153)		
	Recumbent	Standing	P	Recumbent	Standing	P
II (20 to 24 + 6 weeks)	3 (2.2)	20 (14.5)	< 0.001	12 (7.8)	32 (20.9)	< 0.001
III (25 to 29 + 6 weeks)	11 (8.0)	29 (21.0)	< 0.001	25 (16.3)	58 (37.9)	< 0.001

Differences between the two positions in each time interval were assessed with McNemar's test.

Table 4 Stepwise forward multiple logistic regression analysis of cervical length (CL) and funnel width (FW) parameters obtained by transvaginal sonography of the cervix which either reduce (CL) or increase (FW) the risk of spontaneous preterm birth

Implied variables	Singleton pregnancies			Twin pregnancies		
	P	OR	95% CI	P	OR	95% CI
CL st II	0.010	0.920	0.860–0.980	0.001	1.080	1.030–1.130
FW st II						
CL re II						
FW re II						
FW Δ st–re II	0.026	1.080	1.010–1.150	0.006	1.110	1.030–1.190
CL Δ re–st II						
CL st II	0.010	0.920	0.860–0.980	0.001	1.080	1.030–1.130
FW st II						
CL re II						
FW re II						
CL Δ re I–II						
CL Δ st I–II						
FW Δ re II–I						
FW Δ st II–I						

All variables implied in three different combinations of the regression model are listed in the left column; parameters reaching significance within a certain combination of variables for either singleton or twin pregnancies are printed in bold. I, 15 to 19 + 6 weeks; II, 20 to 24 + 6 weeks; OR, odds ratio.

significantly predicted SPB (Table 4). When all absolute values and differences between positions and longitudinal measurements were considered, the results resembled the first step: only absolute values of CL and FW in the upright position significantly predicted SPB (Table 4).

Sensitivity, specificity, PPV, NPV, LR and DOR were analyzed for all described intervals, but only results from examinations performed between 20 and 25 weeks (Group II) are shown in Table 5. Again, the prediction of SPB was improved by considering FW in the upright compared with the recumbent maternal position, independent of the cut-off values. This was not observed for CL. The implementation of calculations of differences between both positions and different longitudinal measurements of either CL or FW did not seem to improve the prediction of SPB within our study population up to 25 weeks.

ROC analysis was therefore performed only for absolute measurements (Figures 1 and 2). In contrast to the logistic regression model, CL between 20 and 25 weeks reached significance in both the recumbent (area under the curve (AUC), 0.665; $P = 0.043$ for singleton, and AUC, 0.673; $P = 0.005$ for twin pregnancies) and the standing (AUC, 0.690; $P = 0.020$ for singleton, and AUC, 0.666; $P = 0.007$ for twin pregnancies) maternal positions, without systematic differences between upright and supine positions (Figure 1a and b). ROC analysis demonstrated that FW between 20 and 25 weeks for the standing maternal position was a better predictor of SPB than was FW for the recumbent maternal position, independent of the cut-off value (Figure 2a and b).

Between 25 and 30 weeks, all areas under the curve for CL and FW increased in comparison to the earlier period, demonstrating better prediction of SPB (Figures 1c, 1d, 2c and 2d), although the prediction of SPB by CL still did not

reveal systematic differences (Figure 1c and d). For FW, the prediction of SPB depended on the cut-off values: a small opening of the internal os detected in the recumbent maternal position may be more indicative of SPB compared with the same value in the standing position. This explains the crossing of the ROC curves. However, the AUCs were still larger for the upright vs. the recumbent position (AUC, 0.768; $P = 0.002$ vs. AUC, 0.674; $P = 0.040$ for singleton pregnancies and AUC, 0.736; $P < 0.001$ vs. AUC, 0.655; $P = 0.012$ for twin pregnancies).

DISCUSSION

Preterm ripening of the cervix reflects a change in its biochemical and mechanical properties^{1–4}. Screening for SPB by TVS is not yet routine in the clinical setting¹⁶. Accordingly, all examinations of singleton pregnancies in this study were performed only in those at risk for SPB. Twin pregnancies carrying a six- to eight-fold risk for SPB were analyzed separately.

Sonographic measurements of the cervix predict SPB better than does digital examination¹⁷. Transabdominal ultrasound requires a full bladder, which may influence the results falsely¹⁸. Transperineal-derived images have been shown to be inadequate in more than 50% of cases, while patient acceptability was similar compared with TVS¹⁹, which was introduced 15 years ago in singleton and later in multiple pregnancies^{9,20,21}.

The stimulus to perform this study was the observation of a 'dynamic opening of the internal os' during or immediately after standing in high-risk patients²². Clinical examination in the upright position was performed during the 19th century because it allowed 'discrete' examination of the pelvis and cervix. At that time, women usually wore a long skirt. The perception of what is acceptable may vary between times and cultures. Even though the fashion

Table 5 Diagnostic indices, positive and negative predictive values (PPV and NPV), likelihood ratios (LR) with 95% CI and diagnostic odds ratio (DOR) stratified for singleton and twin pregnancies, cervical length (CL) and funnel width (FW) with women standing (st) or recumbent (re), the difference between both positions and longitudinal differences of CL and FW between examinations using several cut-off levels (in mm)

Variables/cut-off values	Singleton pregnancies						Twin pregnancies											
	Sensitivity	Specificity	PPV	NPV	LR+	95% CI	LR-	95% CI	DOR	Sensitivity	Specificity	PPV	NPV	LR+	95% CI	LR-	95% CI	DOR
CL re II																		
15 mm	3	100	50	89	8.27	0.17-40.56	0.97	0.88-1.07	8.52	5	99	50	82	4.39	0.47-40.68	0.96	0.88-1.05	4.58
20 mm	3	99	25	89	2.76	0.12-64.65	0.98	0.89-1.08	2.82	9	99	63	83	7.32	1.01-53.14	0.92	0.82-1.04	7.94
25 mm	10	98	38	90	4.96	0.70-34.93	0.92	0.77-1.09	5.40	13	97	50	83	4.39	1.06-18.24	0.90	0.78-1.04	4.88
30 mm	23	96	44	91	6.43	1.77-23.36	0.80	0.60-1.05	8.08	23	91	36	84	2.48	1.04-5.93	0.85	0.69-1.05	2.93
CL st II																		
15 mm	3	100	50	89	8.27	0.17-40.56	0.97	0.88-1.07	8.52	9	98	50	83	4.39	0.80-24.15	0.93	0.83-1.05	4.73
20 mm	10	97	30	90	3.54	0.57-22.22	0.93	0.78-1.10	3.83	23	96	54	85	5.19	1.80-14.97	0.80	0.65-0.99	6.46
25 mm	17	96	31	90	3.76	0.93-15.17	0.87	0.69-1.10	4.31	30	88	37	85	2.58	1.23-5.40	0.79	0.61-1.02	3.26
30 mm	43	91	36	93	4.67	2.10-10.39	0.62	0.40-0.98	7.48	45	87	43	87	3.33	1.81-6.12	0.64	0.46-0.90	5.21
CL Δ re-st II																		
5mm	50	79	24	92	2.41	1.24-4.70	0.63	0.36-1.10	3.83	36	73	21	85	1.34	0.67-2.71	0.87	0.60-1.26	1.53
CL re ΔI-II																		
5 mm	43	79	20	92	2.03	1.04-3.96	0.72	0.46-1.13	2.81	55	62	25	86	1.46	0.98-2.19	0.72	0.47-1.11	2.04
10 mm	23	91	23	91	2.52	0.86-7.33	0.85	0.64-1.12	2.98	41	87	41	87	3.06	1.63-5.76	0.68	0.50-0.93	4.50
15 mm	17	98	50	91	8.27	1.56-43.88	0.85	0.68-1.07	9.72	16	94	38	83	2.64	0.88-7.87	0.89	0.76-1.06	2.95
CL st ΔI-II																		
5 mm	63	67	19	94	1.89	1.20-2.99	0.55	0.28-1.08	3.43	70	65	31	90	1.97	1.40-2.77	0.47	0.26-0.84	4.19
10 mm	37	87	26	92	2.91	1.29-6.55	0.72	0.49-1.07	4.02	48	83	39	88	2.76	1.60-4.75	0.63	0.44-0.91	4.40
15 mm	17	96	31	90	3.76	0.93-15.17	0.87	0.69-1.10	4.31	34	92	50	86	4.39	1.97-9.78	0.72	0.55-0.94	6.14
FW re II																		
5 mm	3	97	13	89	1.18	0.06-21.77	0.99	0.90-1.10	1.19	16	94	38	83	2.64	0.88-7.87	0.89	0.76-1.06	2.95
10 mm	3	97	13	89	1.18	0.06-21.77	0.99	0.90-1.10	1.19	16	95	41	83	3.04	0.98-9.41	0.89	0.75-1.05	3.43
FW st II																		
5 mm	43	88	31	93	3.71	1.74-7.88	0.64	0.41-1.00	5.77	45	83	38	87	2.68	1.51-4.74	0.66	0.47-0.94	4.03
10 mm	37	90	31	92	3.64	1.56-8.49	0.70	0.48-1.04	5.16	45	84	39	87	2.82	1.58-5.03	0.66	0.47-0.93	4.28
FW Δ st-re II																		
5 mm	42	88	32	92	3.64	1.58-8.40	0.65	0.41-1.05	5.58	42	86	38	88	3.03	1.43-6.43	0.68	0.45-1.01	4.49
FW re ΔII-I																		
5 mm	3	97	13	89	1.18	0.06-21.77	0.99	0.90-1.10	1.19	16	96	45	83	3.59	1.11-11.65	0.88	0.74-1.04	4.09
10 mm	3	97	13	89	1.18	0.06-21.77	0.99	0.90-1.10	1.19	16	96	45	83	3.59	1.11-11.65	0.88	0.74-1.04	4.09
15 mm	3	98	17	89	1.65	0.08-32.84	0.99	0.90-1.09	1.68	13	99	70	83	10.25	1.58-66.38	0.89	0.77-1.02	11.57
FW st ΔII-I																		
5 mm	43	89	33	93	3.98	1.85-8.57	0.64	0.41-0.99	6.26	45	86	42	87	3.14	1.72-5.71	0.65	0.46-0.91	4.86
10 mm	37	91	32	92	3.95	1.67-9.38	0.70	0.47-1.03	5.66	38	87	39	86	2.80	1.45-5.39	0.72	0.54-0.97	3.87
15 mm	37	93	39	92	5.35	2.11-8.55	0.68	0.46-1.00	7.87	27	91	42	85	3.14	1.35-7.29	0.80	0.64-1.01	3.92

I, 15 to 19 + 6 weeks; II, 20 to 24 + 6 weeks.

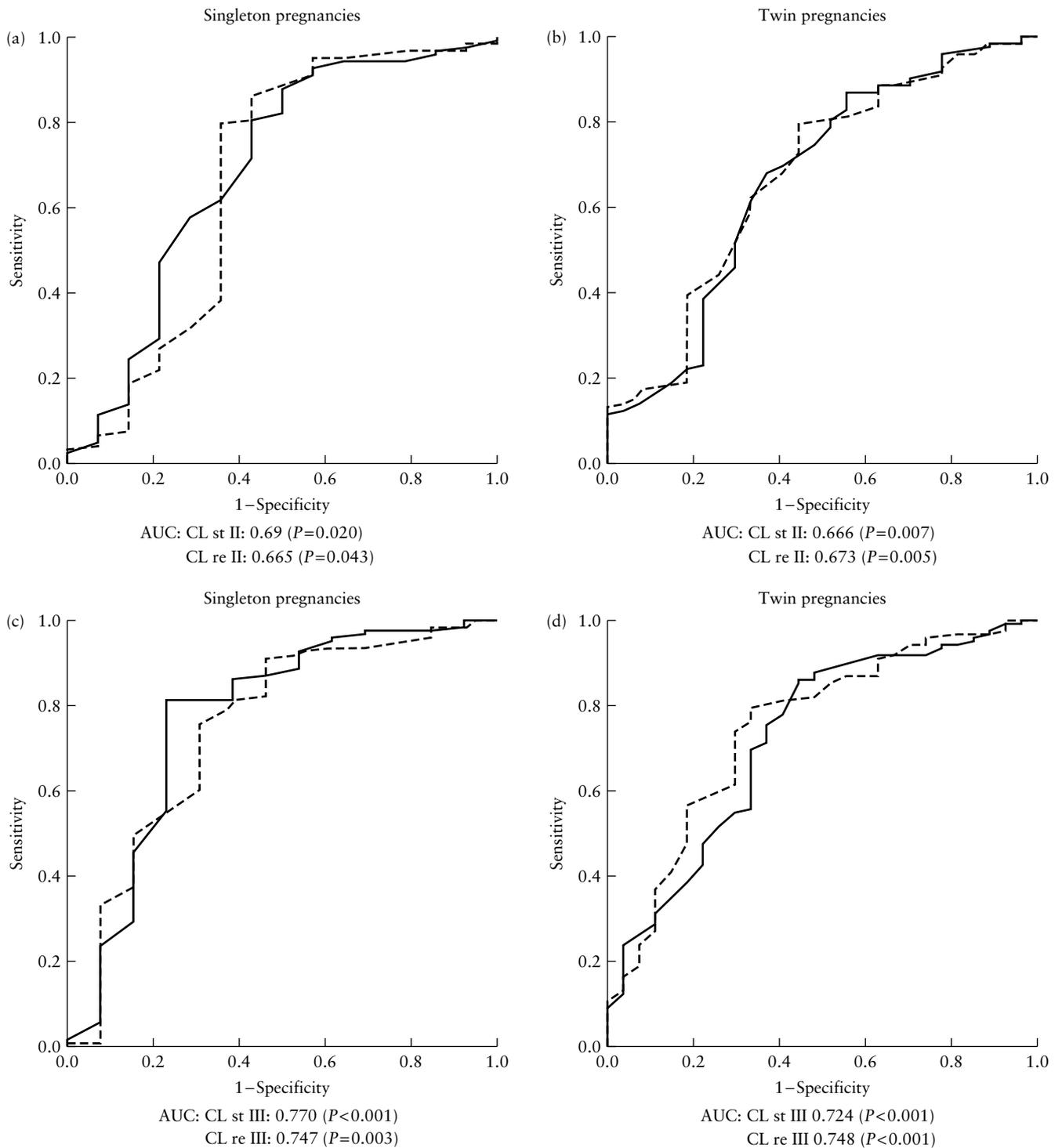


Figure 1 Receiver–operating characteristics curves for cervical length (CL) in both the recumbent (re, dashed line) and the standing (st, solid line) maternal positions for different periods of examination: II, 20 to 24 + 6 weeks (a,b) and III, 25 to 29 + 6 weeks (c,d), separate for 138 singleton (a,c) and 153 twin (b,d) pregnancies. Areas under curves (AUC) are indicated in the figure.

has changed, we have never had difficulties in explaining to our patients why we perform TVS in both positions.

Until now maternal postural challenge during TVS has been performed by only a few groups^{11,22,23}. Instead, transfundal pressure was introduced by Guzman *et al.*¹¹ in the US as a ‘challenge test’ for the cervix during TVS. They compared it with TVS in the standing position in patients at risk for SPB and pregnancy loss,

concluding that transfundal pressure was more effective in eliciting cervical changes. Our experience differed as we observed a series of patients without funneling under transfundal pressure but with funneling when standing (Figure 3). We agree with Guzman *et al.* that in some patients CL increases in the standing position but we did not observe this in patients at risk for SPB unless contractions arose in the recumbent position. Patients may

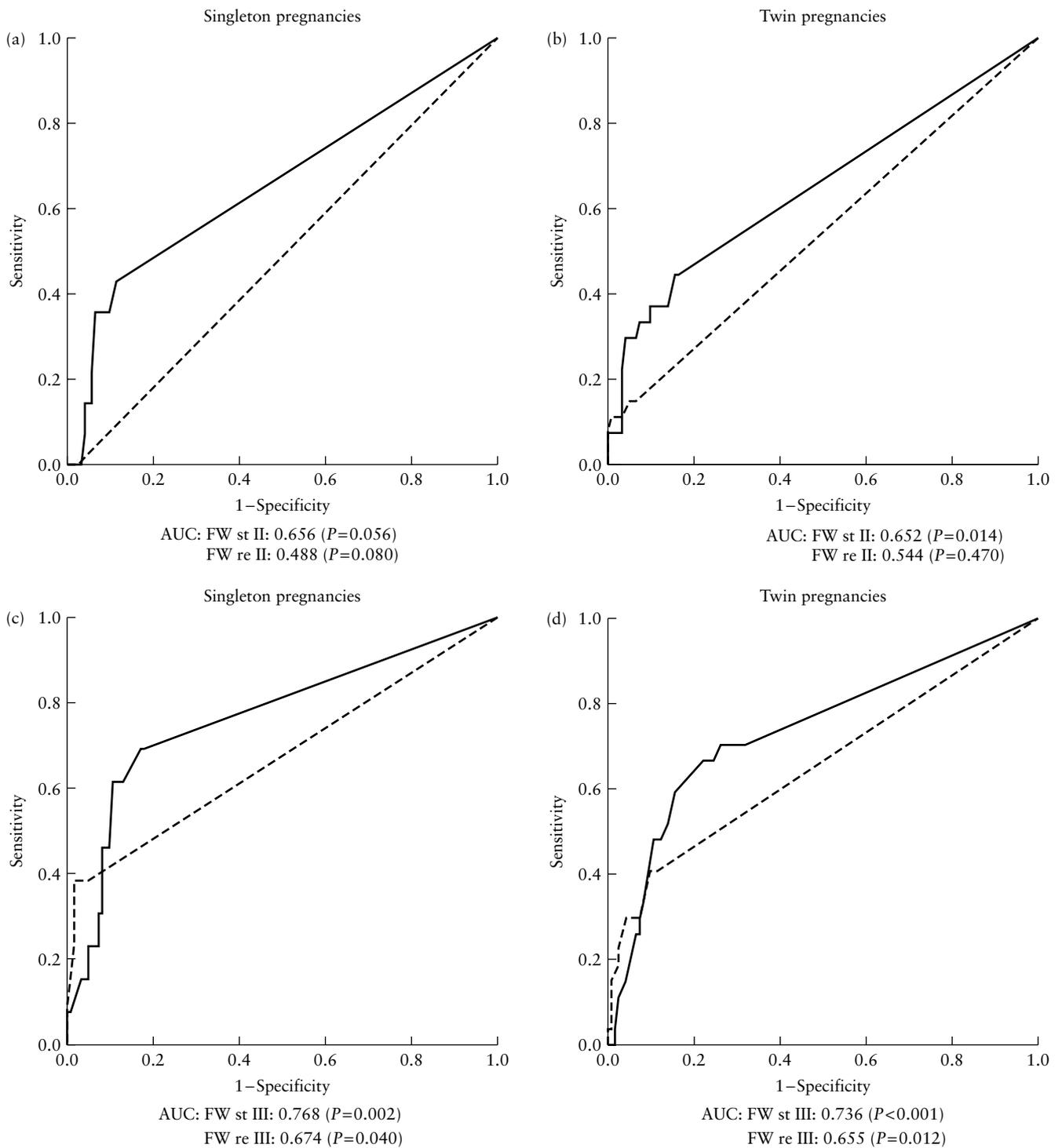


Figure 2 Receiver–operating characteristics curves for funneling width (FW) in both the recumbent (re, dashed line) and the standing (st, solid line) maternal positions for different periods of examination: II, 20 to 24 + 6 weeks (a,b) and III, 25 to 29 + 6 weeks (c,d), separate for 138 singleton (a,c) and 153 twin (b,d) pregnancies. Areas under curves (AUC) are indicated in the figure.

even experience transfundal pressure as uncomfortable, although this differs between examiners. The upright position, however, is a natural posture for the patient during daytime.

In order to prove that TVS can be learned within a short audit period a young researcher was selected as the second examiner for calculation of the intra- and interobserver agreement. It has been stated that even

among experienced observers there may be substantial intra- and interobserver variability in CL and FW measurement^{24,25}. Our results showed good agreement between the two observers; both intra- and interobserver variation were even lower in the group with a short CL (data not shown), for whom diagnostic accuracy is crucial as compared with those with a long endocervical canal.

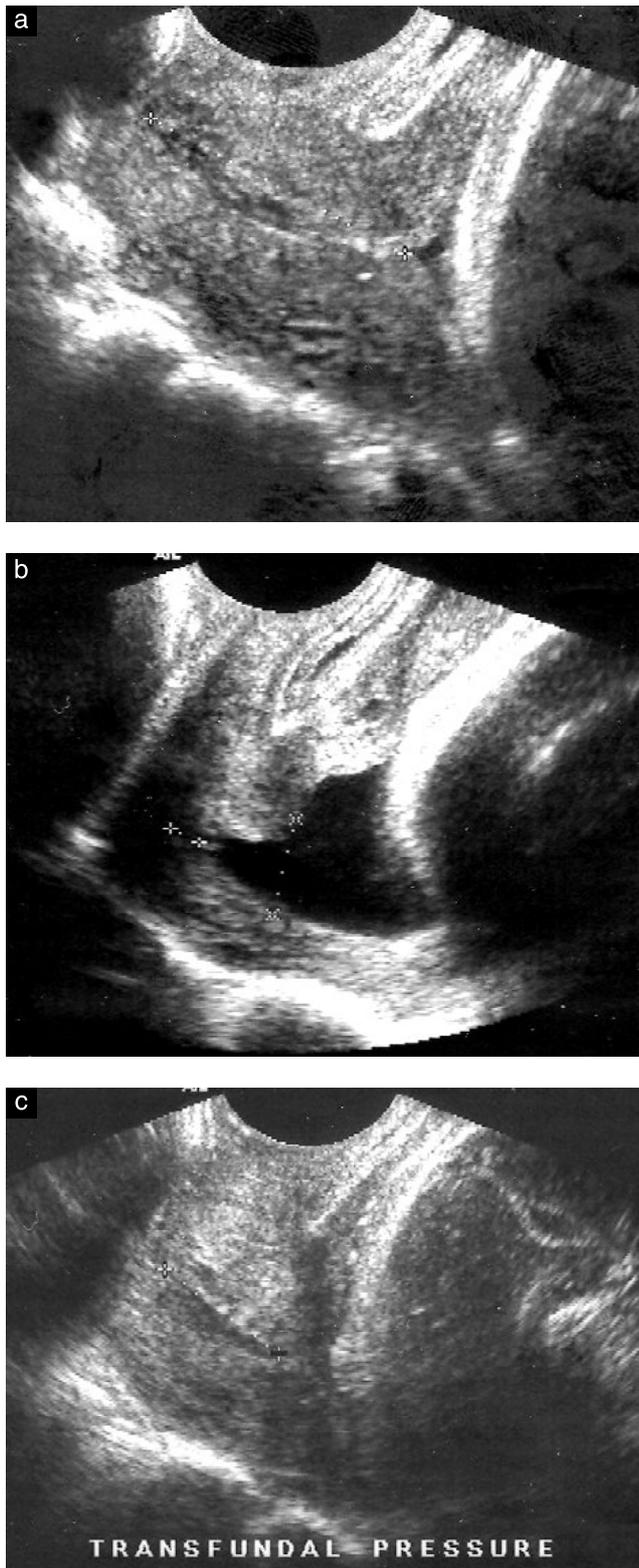


Figure 3 Transvaginal sonography of the cervix within one patient; a) cervix in the recumbent position, b) cervix in the upright position (after 1 min), c) cervix with transfundal pressure.

With regard to the detection of SPB we are aware of the potential weaknesses of our statistics. Within our stepwise forward multiple logistic regression model, the close relationships between covariates and the relatively

low incidence of the outcome of interest (SPB) were limiting factors causing susceptibility to overestimation and type-1 error. We therefore added calculations of diagnostic indices and ROC analysis. Nevertheless, we are aware of the fact that even calculations of LR, DOR and ROC analysis can be biased as obstetricians are rarely blinded to TVS results. Their intention to prevent SPB in patients with pathological results is ethically justified but can increase the false-positive rate if the treatment is successful. However, these errors are part of many studies dealing with the diagnosis of SPB.

Several authors have demonstrated an association between a single ('snapshot') measurement of a short cervix and SPB in low- and high-risk patients^{9,26-29}. The diagnostic accuracy also depends on the gestational age, the applied cut-off values, whether there are additional symptoms of SPB, and whether the pregnancies are singleton or multiple¹⁰. In our study, we did not differentiate between 'symptomatic' or 'asymptomatic', but between different positions, which is easier to define and categorize. Although short values of the CL at early gestation (<20 weeks) have a high predictive value for SPB, reflected by the LR, the sensitivity is low due to the low incidence of such early cervical changes.

Longitudinal examinations have been performed in high-risk patients^{13,14}. Guzman *et al.*³⁰ established rates of CL shortening from 15 weeks onwards to demonstrate that a rapid change reflects the degree of incompetence. In patients with an incompetent cervix, shortening between 20 and 24 weeks varied from 4.9 to 8 mm, which is the rate between 15 weeks to term in normal pregnancies. Accordingly, we analyzed the mean differences of CL in the recumbent position within our gestational age Groups II and III. Among mothers who later presented with SPB, the mean change was 7.2 mm in singleton and 7.9 mm in twin pregnancies. Mothers without SPB only revealed changes of 2.3 mm and 4 mm, respectively. However, the calculation of differences of CL between time interval I and II or between II and III detected only a small percentage of SPB and did not improve the detection rate of SPB either by the multivariate regression model or by our contingency tables. This might depend on characteristics of our study population. Only when longitudinal differences between Groups I and III (25 and 30 weeks) were calculated, were the sensitivity, LR and DOR higher for longitudinal differences compared with single values of CL in Group III (data not shown). It may be interpreted with caution that longitudinal measurements of the CL are still of value in at-risk populations not only to detect any risk as early as possible but also to detect individual change rates for longer intervals.

Our main results between 20 and 25 weeks suggest that a single examination in both positions can exclude or predict SPB with a higher accuracy than can examining a patient in a recumbent position once or even several times. This may have an impact on public health concepts. The fact that patients can correlate sonographic pictures with their own complaints helps to convince them when

lifestyle changes, hospitalization or intervention^{31–33} are indicated or not necessary.

Until now, results of interventional studies have been based on conventional TVS. However, in some patients with singleton pregnancies at risk for SPB and even more so in twin pregnancies, an upright maternal position may allow earlier recognition of an opening of the internal os, protrusion of membranes or even a dissociation of amnion and chorion³⁴. In such pregnancies, a cerclage might actually induce the risk of preterm premature rupture of membranes (PPROM)³⁵ and SPB as suggested for twin pregnancies by a recent meta-analysis³⁶. However, there will still remain patients with a reasonable indication for a cerclage, as shown by a meta-analysis using individual patient-level data³⁶, although the membranes may still descend to the level of the suture, indicating an increased postoperative risk for SPB³⁷. An opening of the internal os and descent of membranes after vaginal cerclage are recognized earlier with the woman in an upright position³⁴.

Rust *et al.*³⁸ published a matched control study of patients with the same CL either with or without funneling. The group with funneling had a higher risk of readmission (67.1% vs. 43.2%), chorioamnionitis (23.2% vs. 2.4%), abruption (13.4% vs. 1.2%) and PPRM (23.4% vs. 6.1%); the neonates in the 'no funnel' group delivered later and had decreased morbidity and mortality. It was recommended that future intervention studies should control for the influence of the discontinuation of the internal os.

It has been reported that prolonged standing provokes uterine contractions to compensate for the decreased venous return in order to maintain normal maternal hemodynamics³⁹. The increase of FW in the upright position may be caused by an interaction of uterine contractility, overdistension, downward pressure and mechanical or biochemical processes of the tissue and membranes at the internal os⁵.

This study underlines the significance of clinical reports of a dilated internal os and the impact of public health measures to reduce physical stress on the rate of SPB within a given population^{40,41}. Since the mechanical properties of the cervical tissue in SPB resemble the changes at term, TVS in both positions may be indicated in patients around term to predict the course of induction and of delivery. Future trials may investigate whether TVS in both positions is advantageous as a routine approach in patients at risk for cervical incompetence and SPB or for cervical dystocia and even to control for intervention to prevent SPB or to induce labor.

REFERENCES

- van Dessel HJ, Frijs JH, Kok FT, Wallenburg HC. Ultrasound assessment of cervical dynamics during the first stage of labor. *Eur J Obstet Gynecol Reprod Biol* 1994; 53: 123–127.
- Rorie DK, Newton M. Histologic and chemical studies of the smooth muscle in the human cervix and uterus. *Am J Obstet Gynecol* 1967; 99: 466–469.
- Uldbjerg N, Ulmsten U. The physiology of cervical ripening and cervical dilatation and the effect of abortifacient drugs. *Baillieres Clin Obstet Gynaecol* 1990; 4: 263–282.
- Breeveld-Dwarkasing VN, te Koppele JM, Bank RA, van der Weijden GC, Taverne MA, van Dissel-Emiliani FM. Changes in water content, collagen degradation, collagen content, and concentration in repeated biopsies of the cervix of pregnant cows. *Biol Reprod* 2003; 69: 1608–1614.
- Romero R, Mazor M, Munoz H, Gomez R, Galasso M, Sherer DM. The preterm labor syndrome. *Ann N Y Acad Sci* 1994; 734: 414–429.
- Romero R, Sirtori M, Oyarzun E, Avila C, Mazor M, Callahan R, Sabo V, Athanassiadis AP, Hobbins JC. Infection and labor. V. Prevalence, microbiology, and clinical significance of intraamniotic infection in women with preterm labor and intact membranes. *Am J Obstet Gynecol* 1989; 161: 817–824.
- Romero R, Shamma F, Avila C, Jimenez C, Callahan R, Nores J, Mazor M, Brekus CA, Hobbins JC. Infection and labor. VI. Prevalence, microbiology, and clinical significance of intraamniotic infection in twin gestations with preterm labor. *Am J Obstet Gynecol* 1990; 163: 757–761.
- Romero R, Espinoza J, Mazor M. Can endometrial infection/inflammation explain implantation failure, spontaneous abortion, and preterm birth after in vitro fertilization? *Fertil Steril* 2004; 82: 799–804.
- Andersen HF, Nugent CE, Wanty SD, Hayashi RH. Prediction of risk for preterm delivery by ultrasonographic measurement of cervical length. *Am J Obstet Gynecol* 1990; 163: 859–867.
- Honest H, Bachmann LM, Coomarasamy A, Gupta JK, Kleijnen J, Khan KS. Accuracy of cervical transvaginal sonography in predicting preterm birth: a systematic review. *Ultrasound Obstet Gynecol* 2003; 22: 305–322.
- Guzman ER, Rosenberg JC, Houlihan C, Ivan J, Waldron R, Knuppel R. A new method using vaginal ultrasound and transfundal pressure to evaluate the asymptomatic incompetent cervix. *Obstet Gynecol* 1994; 83: 248–252.
- Sherif LS, Shalan HM. Detection of pregnant women at risk of cervical incompetence by transvaginal sonography during straining. *J Obstet Gynaecol Res* 1997; 23: 353–357.
- Arabin B, van Eyck J. Sonographic diagnosis of cervical incompetence for prevention and management. *Ultrasound Review* 2001; 1: 1–10.
- Arabin B, Hübener M, Halbesma JR, van Eyck J. Sonographic diagnosis of cervical incompetence in twin pregnancies. *Ultrasound Review* 2001; 1: 340–349.
- Lijmer JG, Mol BW, Heisterkamp S, Bossel GJ, Prins MH, van der Meulen JH, Bossuyt PM. Empirical evidence of design-related bias in studies of diagnostic tests. *JAMA* 1999; 282: 1061–1066.
- Iams JD. Prediction and early detection of preterm labor. *Obstet Gynecol* 2003; 101: 402–412.
- Gomez R, Galasso M, Romero R, Mazor M, Sorokin Y, Goncalves L, Treadwell M. Ultrasonographic examination of the uterine cervix is better than cervical digital examination as a predictor of the likelihood of premature delivery in patients with preterm labor and intact membranes. *Am J Obstet Gynecol* 1994; 171: 956–964.
- To MS, Skentou C, Cicero S, Nicolaides KH. Cervical assessment at the routine 23-week scan: problems with transabdominal sonography. *Ultrasound Obstet Gynecol* 2000; 15: 292–296.
- Cicero S, Skentou C, Souka A, To MS, Nicolaides KH. Cervical length at 22–24 weeks of gestation: comparison of transvaginal and transperineal-translabial ultrasonography. *Ultrasound Obstet Gynecol* 2001; 17: 335–340.
- Guzman ER, Walters C, O'Reilly-Green C, Kinzler WL, Waldron R, Nigam J, Vintzileos AM. Use of cervical ultrasonography in prediction of spontaneous preterm birth in twin gestations. *Am J Obstet Gynecol* 2000; 183: 1103–1107.
- Guzman ER, Walters C, O'Reilly-Green C, Meirowitz NB, Gipson K, Nigam J, Vintzileos AM. Use of cervical ultrasonography

- in prediction of spontaneous preterm birth in triplet gestations. *Am J Obstet Gynecol* 2000; **183**: 1108–1113.
22. Arabin B, Aardenburg R, van Eyck J. Maternal position and ultrasonic cervical assessment in multiple pregnancy. Preliminary observations. *J Reprod Med* 1997; **42**: 719–724.
 23. Wong G, Levine D, Ludmir J. Maternal postural challenge as a functional test for cervical incompetence. *J Ultrasound Med* 1997; **16**: 169–175.
 24. Burger M, Weber-Rössler T, Willmann M. Measurement of the pregnant cervix by transvaginal sonography: An inter-observer study and new standards to improve inter-observer variability. *Ultrasound Obstet Gynecol* 1997; **9**: 188–193.
 25. Valentin L, Bergelin I. Intra- and interobserver reproducibility of ultrasound measurements of cervical length and width in the second and third trimesters of pregnancy. *Ultrasound Obstet Gynecol* 2002; **20**: 256–262.
 26. Heath VC, Southall TR, Souka AP, Novakov A, Nicolaides KH. Cervical length at 23 weeks of gestation: relation to demographic characteristics and previous obstetric history. *Ultrasound Obstet Gynecol* 1998; **12**: 304–311.
 27. Iams JD, Paraskos J, Landon MB, Teteris JN, Johnson FF. Cervical sonography in preterm labor. *Obstet Gynecol* 1994; **84**: 40–46.
 28. Hassan SS, Romero R, Berry SM, Dang K, Blackwell SC, Treadwell MC, Wolfe HM. Patients with an ultrasonographic cervical length ≤ 15 mm have nearly a 50% risk of early spontaneous preterm delivery. *Am J Obstet Gynecol* 2000; **182**: 1458–1467.
 29. Timor-Tritsch IE, Boozarjomehri F, Masakowski Y, Monteagudo A, Chao CR. Can a “snapshot” sagittal view of the cervix by transvaginal ultrasonography predict active preterm labor? *Am J Obstet Gynecol* 1996; **174**: 990–995.
 30. Guzman ER, Mellon C, Vintzileos AM, Ananth CV, Walters C, Gipson K. Longitudinal assessment of endocervical canal length between 15 and 24 weeks’ gestation in women at risk for pregnancy loss or preterm birth. *Obstet Gynecol* 1998; **92**: 31–37.
 31. Althuisius S, Dekker G, Hummel P, Bekedam D, Kuik D, van Geijn H. Cervical Incompetence Prevention Randomized Cerclage Trial (CIPRACT): Effect of therapeutic cerclage with bed rest vs. bed rest only on cervical length. *Ultrasound Obstet Gynecol* 2002; **20**: 163–167.
 32. To MS, Alfirevic Z, Heath VC, Cicero S, Cacho AM, Williamson PR, Nicolaides KH; Fetal Medicine Foundation Second Trimester Screening Group. Cervical cerclage for prevention of preterm delivery in women with short cervix: randomised controlled trial. *Lancet* 2004; **363**: 1849–1853.
 33. Arabin B, Halbesma JR, Vork F, Hubener M, van Eyck J. Is treatment with vaginal pessaries an option in patients with a sonographically detected short cervix? *J Perinat Med* 2003; **31**: 122–133.
 34. Arabin B, Nizard J, van Eyck J. Pregnancy management: assessment of cervical status. In *Multiple Pregnancy. Epidemiology, Gestation & Perinatal Outcome*, Blickstein I, Keith L (eds). Taylor & Francis, A Parthenon Book: London & New York, 2005; 456–469.
 35. Hassan SS, Romero R, Maymon E, Berry SM, Blackwell SC, Treadwell MC, Tomlinson M. Does cervical cerclage prevent preterm delivery in patients with a short cervix? *Am J Obstet Gynecol* 2001; **184**: 1325–1329; discussion 1329–1331.
 36. Berghella V, Odibo AO, To MS, Rust OA, Althuisius SM. Cerclage for short cervix on ultrasonography: meta-analysis of trials using individual patient-level data. *Obstet Gynecol* 2005; **106**: 181–189.
 37. O’Brien JM, Hill AL, Barton JR. Funneling to the stitch: an informative ultrasonographic finding after cervical cerclage. *Ultrasound Obstet Gynecol* 2002; **20**: 252–255.
 38. Rust OA, Atlas RO, Kimmel S, Roberts WE, Hess LW. Does the presence of a funnel increase the risk of adverse perinatal outcome in a patient with a short cervix? *Am J Obstet Gynecol* 2005; **192**: 1060–1066.
 39. Schneider KT, Bung P, Weber S, Huch A, Huch R. An orthostatic uterovascular syndrome—a prospective, longitudinal study. *Am J Obstet Gynecol* 1993; **169**: 183–188.
 40. Papiernik E, Bouyer J, Collin D. Prevention of preterm births: a perinatal study in Haguenau, France. *Pediatrics* 1985; **76**: 154–158.
 41. Papiernik E, Bouyer J, Collin D, Winisdoerffer G, Dreyfus J. Precocious cervical ripening and preterm labor. *Obstet Gynecol* 1986; **67**: 238–242.