

THE ASSOCIATION BETWEEN CERVICAL SONOGRAPHY AND SUCCESSFUL INDUCTION OF LABOR: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Many sonographic assessments of the cervix have been introduced to assess pre-induction cervical ripening for vaginal delivery (VD). However, the association between existing cervical assessments and successful VD remains unclear. This systematic review was conducted to estimate and compare the association between existing cervical assessments and successful VD in pregnant women who underwent induction of labor (IOL). Related studies were identified from PubMed, EMBASE, and Scopus from inception to July 2022. A multi-level mixed-effects logistic regression model was applied to estimate the odds ratio (OR) of successful VD and compare association among cervical assessments by relative ORs. A total of 86 studies which comprised 13,797 patients were included. The results showed that all cervical assessments (i.e., cervical length (CL), cervical wedging, cervical funneling, cervical elastography, uterocervical angle (UCA), and cervical volume) had a significant association with VD with OR (95% confidence interval (CI) of 4.89 (4.41, 5.42), 2.68 (2.16, 3.32), 1.63 (1.10, 2.43), 1.70 (1.12, 2.57), 4.52 (3.57, 6.72), and 6.13 (2.57, 14.62), respectively. The cervical volume was the highest association with a relative OR of 1.26 (0.52, 3.01) when compared with CL, but non-statistical significance. The rest of the cervical assessments showed lower association when compared with CL.

Keywords: Induction of Labor, Sonographic Cervical Assessment, Cervical Length

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INTRODUCTION

Induction of labor (IOL) is one of the most common procedures in many countries with prevalence ranging from 1.4-35%. (GETAHUN, 2014; Marconi, 2019). In 2020, the prevalence of IOL was reported as 4.5% in Ramathibodi Hospital in Bangkok, Thailand (Kamlungkuea, Manonai, Suriyawongpaisal, & Hansahiranwadee, 2022). In clinical practice, IOL should be considered when the benefits to either the mother or fetus outweigh the risk of pregnancy continuation and awaiting spontaneous onset labor (SMFM Statement on Elective Induction of Labor in Low-Risk Nulliparous Women at Term: the ARRIVE Trial, 2019).

The benefit of IOL has been well established to improve maternal and fetal outcomes ("ACOG Practice Bulletin No. 107: Induction of labor," 2009; Cunningham et al., 2022). IOL leads to higher rates of chorioamnionitis (20-27%) and postpartum hemorrhage (PPH) (11-16%) which have been reported after 6 and 12 hours of the latent phase, respectively. (Kamlungkuea et al., 2022). In addition, IOL can cause uterine hyperstimulation in pregnant women which increases the chance of emergency cesarean delivery (CD) as well as causes fetal heart rate (FHR) changes and fetal compromise (1-5%) (Ben-Haroush et al., 2004; Seyb, Berka, Socol, & Dooley, 1999; Vrouenraets et al., 2005; Zlatnik, 1999).

The cervical status has favorable characteristics in terms of readiness to enter the labor state which appear to exert the most important influence on the outcome of IOL. (Baacke & Edwards, 2006; Hatfield, Sanchez-Ramos, & Kaunitz, 2007). Many sonographic assessments of the cervix have been introduced to assess pre-induction cervical ripening that responds to VD. However, the association between different pre-induction sonographic cervical assessments with successful IOL is still unknown in clinical practice. Therefore, this systematic review and meta-analysis (SRMA) aimed to estimate the association between sonographic cervical assessment and successful IOL and compare the association between them.

LITERATURE REVIEWS

The association between sonographic cervical assessments and successful VD

The common pre-induction cervical assessment method used is the cervical scoring system known as the Bishop Score (BS). According to the previous SRMA (Kolkman et al., 2013; Teixeira, Lunet, Rodrigues, & Barros, 2012) which considered the BS and successful IOL showed a positive association with vaginal delivery (VD) with odds ratio (OR) and 95% confidence interval (CI) of 1.33 (1.13, 1.56). However, the BS was subjective, unreliable and had high interobserver variance (Buchmann & Libhaber, 2008; Feltovich & Carlson, 2017).

Sonographic assessment of the cervix was subsequently introduced to assess pre-induction cervical ripening. It is preferred over the BS due to its reproducibility and reduced intra and interobserver variability (Hatfield et al., 2007). The cervical length (CL), cervical funneling (representing dilatation), and cervical wedging, which are changes associated with cervical ripening, have been investigated as transvaginal ultrasound (TVS) parameters for predicting successful IOL (Verhoeven et al., 2013). The previous SRMA found that CL predicted successful IOL with a likelihood ratio of a positive test (LR+) and 95% CI of 1.66 (1.20-2.31), sensitivity = 0.64 (0.57-0.71), and specificity = 0.65 (0.55-0.76). Cervical wedging had LR+ of 2.64 (1.79-3.88), sensitivity = 0.44 (0.29-0.66), and specificity = 0.83 (0.75-0.91).

There is also cervical elastography (measured by TVS) which displayed cervical stiffness for predicting cervical ripening and had a diagnostic odds ratio (DOR) for successful VD with 5.24 (3.23-8.50) (Hee, Rasmussen, Schlüter, Sandager, & Uldbjerg, 2014).

Furthermore, the introduction of uterocervical angle (UCA), defined as the angle between the lower uterine segment and the cervical canal, can also be reproducible and measured by TVS (Hassan et al., 2014). Larger UCA is a good predictor of the response to successful IOL because of the additional force the uterus has to exert on the cervix. According to (Yang et al., 2021), UCA had a diagnostic odds ratio (DOR) for successful VD with 4.33 (1.62-11.65).

The alternative novel sonographic cervical assessment is cervical volume, measured by TVS and calculated assuming the cervix as a cylinder in geometric view, has cervical favorability (representing effacement) for predicting successful VD with OR = 1.10 (1.05-1.16) (Athulathmudali, Patabendige, Chandrasinghe, & De Silva, 2021).

Current evidence from previous studies

There were 3 SRMAs that assessed the performance of sonographic cervical assessments for successful IOL. Of those, 2 MAs (Hatfield et al., 2007; Verhoeven et al., 2013) assessed the diagnostic accuracy of CL and cervical wedging in predicting success or failure of IOL, and 1 MA (Londero, Schmitz, Bertozzi, Driul, & Fruscalzo, 2016) evaluated the diagnostic accuracy of cervical elastography in predicting successful IOL. The first SRMA (Hatfield et al., 2007) included 20 studies comprising 3,101 participants, assessing the diagnostic accuracy of CL to predict the successful IOL and found that CL predicted successful IOL with pooled LR+ of 1.66 (1.20-2.31), sensitivity = 0.64 (0.57-0.71), and specificity = 0.65 (0.55-0.76). For cervical wedging, 5 studies were included, with 488 participants had pooled LR+ of 2.64 (1.79-3.88), sensitivity = 0.44 (0.29-0.66), specificity = 0.83 (0.75-0.91). The second SRMA (Verhoeven et al., 2013) assessed the diagnostic performance by a bivariate MA model of CL to predict the failed IOL (CD) which included 31 studies, comprising 5,029 participants. For the prediction of CD, sensitivity ranged from 0.14 to 0.92, and specificity ranged from 0.35 to 1.00. The third SRMA (Londero et al., 2016) determined the diagnostic accuracy of cervical elastography in predicting successful VD. A total of 4 studies involving 323 participants showed that the cervical elastography had an accurate diagnostic odds ratio (DOR) for successful VD with medical IOL = 5.24 (3.23-8.50).

Based on the concept of diagnostic accuracy study (World Health, 2014), all subjects must perform both the index and reference standard tests. However, the successful IOL was not measured by reference standard test, so pooling of diagnostic accuracy might be an inappropriate method. The assessment of the association between each cervical assessment with successful IOL by estimating the OR is a more appropriate approach for this condition.

To date, the questions regarding the highest association among different pre-induction sonographic cervical assessments with successful IOL are still unknown in clinical practice. Therefore, this SRMA aimed to assess the association of all available sonographic cervical assessments with successful IOL and determine which one has the highest association with successful IOL.

RESEARCH METHODOLOGY

Study design

The study design is a SRMA which was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) extension statement for reporting systematic reviews incorporating MAs (Page et al., 2021). This study was registered in PROSPERO number CRD42022352546.

Databases and search strategies:

The relevant studies were identified from MEDLINE via PubMed, EMBASE up to 30th July 2022. The search terms and search strategies were constructed based on patient (pregnant who underwent IOL), study factor (sonographic cervical assessments i.e., CL, cervical wedging, cervical funneling, cervical elastography, UCA, and cervical volume), outcomes of interest (successful VD), and restrictions regarding study design were not applied.

Selection of studies

Any type of cohort studies published in any language were included if they met all the following criteria: studied in pregnant women who underwent IOL, studied that reported sonographic cervical assessments with or without the BS regardless of cut-off value, and studied in successful VD. Studies were excluded if they published in non-English which were

untranslatable languages or had insufficient data for pooling after three contact attempts with authors every two weeks. Identified studies were independently selected by 2 reviewers (M.S. and A.K.) using the information from the title and abstract based on the eligible criteria. Full articles were subsequently reviewed after title and abstract screening.

Data extraction

Data was extracted independently by 2 reviewers (M.S. and A.K.) using a data extraction form (DEF). The DEF consist of general information (i.e., the author, year of publication), study characteristics (i.e., country), general characteristics of participants (e.g., age, body mass index (BMI), Gestational age (GA), parity (nulliparous or multiparous), estimate fetal weight (EFW), the method of IOL (Prostaglandin E1 (PGE1), prostaglandin E2 (PGE2), Foley catheter), the indication of IOL, information about study factors (i.e., the cut-off value of measurement, the technique of measurement, ultrasound machine, number of operators, certification of sonography, and experience of performing), definition of outcomes, and data for pooling. Frequency data or summary statistics (OR) with 95% CI were extracted for data pooling.

Risk of bias assessment

The quality of studies was independently assessed by 2 reviewers (M.S. and A.K.) using the Newcastle Ottawa Scale (NOS) modified (Wells G). Disagreement was solved by discussion with all of the reviewer team. This tool consist of three domains of risk of bias; selection of the representativeness of the studied subjects, the comparability between groups, and the ascertainment of outcome and study factor. Every item consist of a question with three possible answers (yes, no, or unclear). The possible score range was from 0 to 9 stars. Individual studies were categorized, according to these stars, and studies having scores from 7-9 stars were identified a low risk of bias, 4-6 high risk of bias, and 0-3 very high risk of bias.

Statistical analysis

Sonographic cervical assessments were numerically code for CL-long cervix (0), CL-short cervix (1), Cervical funneling-absent (2), Cervical funneling-present (3), Cervical wedging-absent (4), Cervical wedging-present (5), Cervical elastography-stiffness (6), Cervical elastography-soft (7), UCA- narrow angle (8), UCA-wide angle (9), Cervical volume- high volume (10), Cervical volume- low volume (11). Frequency data's combination of cervical assessments with cut-off (positive vs negative) and successful VD (yes vs no) were expanded to individual patient data. A multi-level mixed-effect logistic regression model was applied by fitting sonographic cervical assessments on successful VD. The study level and cut-off value were fitted as random-effect and cervical assessment was fitted as fixed-effect in the model. Then the OR with 95% CI for each cervical assessment were estimated. The comparison of the association between all available sonographic cervical assessments and successful VD was performed to estimate the relative OR between any pair of sonographic cervical assessments. The relative OR can be defined as OR of interesting cervical assessment divided by OR of other sonographic cervical assessment which was set as a reference group. All analyses were performed using STATA software package, version 18.0. (Stata Corp, College Station, Texas, USA). A two-sided p-value of less than 0.05 was considered statistically significant.

RESEARCH RESULTS

Study selection

The selection process was illustrated in Figure 1. The search through literature databases with comprehensive search terms found a total of 2,684 studies, including 1,007 studies from MEDLINE via PubMed, 891 studies from Scopus, and 786 studies from EMBASE. Among these, 837 duplicate studies were removed, leaving 1,848 studies for screening the titles and abstracts. Of these, 1,729 studies were excluded, yielding 118 studies for full-text reviewing, and then 2 studies were excluded from not retrieving full text, resulting in 116 studies for full-text reviewing. Among them, 86 studies met the inclusion criteria.

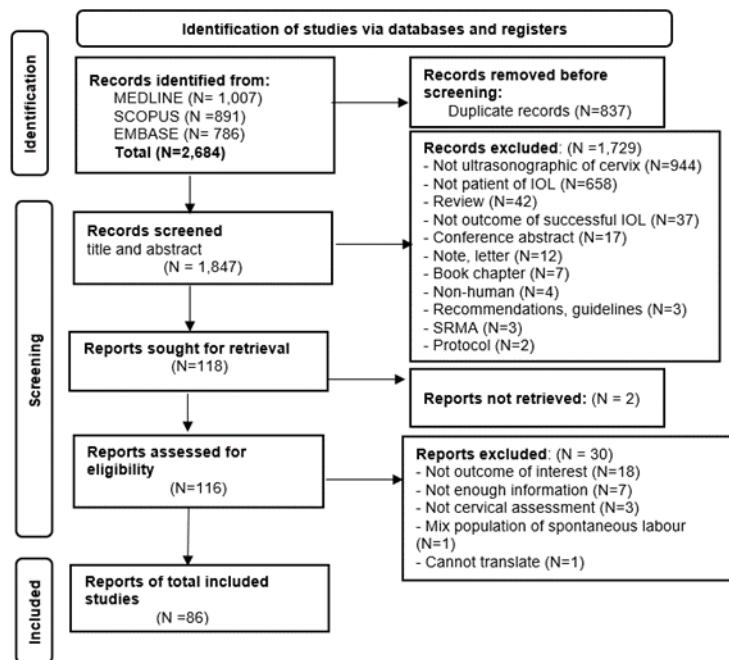


Figure 1 PRISMA Flow diagram (Page et al., 2021)

Characteristics of included studies

This review included 86 cohort studies published between 1998 and 2022 which were comprised of 13,797 pregnancies who underwent IOL. The details of patients' characteristics, and methods of IOL are described in Table 1. The mean age ranged from 21.44 to 40 years. Mean BMI, ranged from 22.62 to 31.67 kg/m². The mean GA ranged from 25.20 to 41.76 weeks. The mean EFW ranged from 2,180 to 3,593.8 grams. Among 70 studies, 19 studies (26.76%) enrolled only nulliparous, 25 studies (35.71%) received only PGE1, 48 studies (68.57%) received only PGE2, and 9 studies (12.86%) used only Foley catheters >50%. Sixteen studies received PGE1 100%, and 40 studies received PGE2 >50%.

Table 1 Characteristics of patients, and methods of IOL of included studies

Author,Year	Mean age (year)	Mean BMI (kg/m ²)	Mean GA (week)	Mean EFW (gram)	Nulliparous (%)	PGE1 (%)	PGE2 (%)	Foley (%)
Paterson Brown, 1991					52			100
Gonen R, 1998	28.40				48			100
Ware V, 2000	40				42	42	0	
Pandis G K, 2001	29.65	28.60	40.6	3593.80	55.17	48.27	51.72	
Pandis G K, 2001	29.70	28.1	41		53.30		100	
Gabriel R, 2002					48.04		100	
Rane S M, 2003				41.42	50.26		100	
Rane S M, 2003	29	27			50.30		100	
Reis F M, 2003	31.96			40.30			100	
Roman H, 2004							64.15	
Yang S H, 2004	27.30			40.50	74		100	
Greco P, 2005	28.42	22.62	40	3412.07	100		100	
Rane S M, 2005	30.55	28.75	39.78		45.90			
Rovas L, 2005	33	30.50			47		100	
Rozenberg P, 2005	29.55			39.60	71			
Caliskan E, 2006	27.50	28	39.20	3311	51.40	100		100
Daskalakis G, 2006	26.15	29.28	39.75	3402.75	100		100	
Elghorori MR, 2006	26.50			41.14	51.40		80.10	
Gomes F, 2006	23.51				68.00		100	
Tan P C, 2006							78.90	
Cromi A, 2007	31.50	27.40	39.70		76.10	100	100	
Gomez Laencina A, 2007	31.22	28.60	39.64		70.10		100	
Keepanasseril A, 2007	26.25	30.23	37.75	2720	100	27.50	28.20	

Table 1 Characteristics of patients, and methods of IOL of included studies (cont.)

Author,Year	Mean age (year)	Mean BMI (kg/m ²)	Mean GA (week)	Mean EFW (gram)	Nulliparous (%)	PGE1 (%)	PGE2 (%)	Foley (%)
Park K H, 2007	30.34		39.33	3245	100		8.6	
Tan P C, 2007	30.26		40.39	3240	43.33		76.30	
Yanik A, 2007	26.70		41.19	3543.03	58.90			
Eggebo T M, 2008	30.75	27.50	40		47	100		
Tanir H M, 2008	26.23	24.78	38.29	3225.67	100	100		
Maitra N, 2009						100		
Meijer-Hoogeveen M, 2009	31	26	41.14		66.66		100	
Park K H, 2009	30.92	28.39	37.68		83		72.20	
Tan P C, 2009	30.17				42.85		76.19	
Uyar Y, 2009	24.19	25.49		3282.04	71			
Verhoeven C J M, 2009	31.21	24.46	40.36		57.90		45	
Cheung C W, 2010	29.40			3381	61.30		28.60	
Sierszewski P, 2010			40.50		73.27			
Aragao J R B F, 2011	24.50		39.60		64.28			
Bastani P, 2011	29.90		39.60		66.66			
Gomez Laencina A M					70.10		100	
Abdelazim I A, 2012	31.99		38.17				48.33	
Hwang H S, 2013	31.50	28.75	40.46	3330	100			
Cubal A, 2013	21.44		40.86	3493.77	61.92		100	
Hwang H S, 2013	31.50	28.75	40.46	3330	100			
Uzun I, 2013	24.67	27.87			100			
Muscatello A, 2014	32.05				62			
Ancel J, 2015	30.75	25.93	39.75		60		100	
Chung S H, 2015	30.90		38.30	3021	100		100	
Fruscalzo A, 2015	29.70		39.70		58		100	
Gokturk U, 2015	23.89	28.80	39.99					
Alvarez-Colomo C, 2016	32.60				68.20		88.2	
Ben-Harush Y, 2016	29		39.80	3248			100	
Kant R H, 2016	24.80	26.30	39		100		100	
Khazardoost S, 2016	25.13	28.8		3334	100	100		
Nikbakht R, 2016	25.50		40.10		72.97			
Prado C A C, 2016	25.50	31.1	40.50		43.62	100		
Uygur D, 2016	23.30	28.10	40.70	3401	100			
Aracic N, 2017	28.51		38.81		49.50		100	
Valikkannu N, 2017	28.83	29.80	39.36	3020	100		100	
Al-Adwy A M, 2018	26.19	26.68			41.42	100		
Aydin A G, 2018	28.69		38.79		57.90		46.80	
Kaoian V, 2018			39.30	3155.70	53.10			
Khandelwal R, 2018					100	100	100	
Mousa B A, 2018	26.10		39.40	3400	66.66	100		
Raynelda F, 2018								
El Mekkawi S, 2019	24.13		38		100	100		
Migliorelli F, 2019	33.72	23.85	40.06	3381	28.51	66.03	27.46	71.69
Servin C E, 2019	24	31.67	41.76	3428.66	67	100		
Anikwe C C, 2020	30.68		39.57	2180	28.30			
Bila J, 2020	28.53	28.45	41.35	3470	100	32.90	33.60	
De Miguel Manso S, 2020	32.93	28.83	39.81		71	100		
Eser A, 2020	25.69	29.09	40.09				100	
Kim Y N, 2020	31.02	27.15	39.16	3163	100		100	
Li X, 2020	29.56		36.83		100			
Mohamed B, 2020	29.65	29.6	39.06		74	100		
Turkyilmaz G, 2020	25.70		25.20		100		100	
Alanwar A, 2021	27.20	27.6	39.40		24.38	100		
Amupala A, 2021	30.55		37.97	3060.57		54	54	
Arthius C, 2021	29	25.50	40.10		60.80		100	
Athulathmudali S R, 2021	29.21	24	40.11	2970	71		100	
El-Maghraby I M, 2021	23.34	29.12	39.85			53.57		
Hamsa A, 2021	30.10	31	39	3401		100	100	
Hassan S S M, 2021	23.99	25.62		3061.43		100		
Rathore A, 2021	23.22	25.97		3030	100	6	94	
Yang S W, 2021		26	39		61		100	
Zhou Y, 2021	29.166	26.38	38	3310			100	
Abdullah Z H A, 2022	29.90	26.88	39.33	3044.99	44.90	100	100	

Assess the association between sonographic cervical assessment and successful VD

Among 86 studies, 73 studies were reported the frequency data of the association between sonographic cervical assessments and successful VD. Seventy-two studies assessed CL (short vs long) with successful VD. The cut-off values ranging from 12.5-43 mm. The short CL was significantly higher odds of successful VD than long CL with estimated OR with 95% CI of 4.89 (4.41, 5.42). Twenty studies assessed cervical funneling (present vs absent) with successful VD. The present funneling was significantly higher odds of successful VD than absent funneling with estimated OR with 95% CI of 2.68 (2.16, 3.32). Two studies assessed cervical wedging (present vs absent). The present wedging was significantly higher odds of successful VD than absent wedging with estimated OR with 95% CI of 1.63 (1.10, 2.43). Five studies assessed cervical elastography (soft vs stiffness). The soft cervix was significantly higher odds of successful VD than stiffness cervix with estimated OR with 95% CI of 1.70 (1.12, 2.57). Thirteen studies assessed UCA (wide vs narrow). The cut-off values ranged from 70-120 degrees. The wide UCA was significantly higher odds of successful VD than narrow UCA with estimated OR with 95% CI of 4.52 (3.57, 6.72). One study assessed cervical volume (low vs high). The low volume was significantly higher odds of successful VD than high volume with estimated OR with 95% CI of 6.13 (2.57, 14.62). Cervical volume had the highest association with successful VD, followed by CL, UCA, cervical funneling, cervical elastography, and cervical wedging, respectively. The results of the association of each sonographic cervical assessment and successful VD are shown in Table 2.

Comparison of the association between different sonographic cervical assessments and successful VD

The comparison of the association between six sonographic cervical assessments and successful VD was performed by estimating the relative OR between any pair of sonographic cervical assessments. Cervical volume had the highest relative OR of 1.26 (0.52, 3.01) with CL, but with non-statistical significance. The remaining cervical assessments showed a lower association with success in VD when compared with CL. The results of the comparison with the relative ORs among the different cervical assessments are shown in table 2.

Table 2 Comparison of the association between different sonographic cervical assessments and VD

Reference cervical assessment	Relative ORs (95%CI)					
	CL	Funneling	Wedging	Elastography	UCA	Volume
CL	4.89 (4.41, 5.42)	0.55 (0.44, 0.69)	0.28 (0.18, 0.44)	0.35 (0.23, 0.53)	0.92 (0.72, 1.21)	1.26 (0.53, 3.04)
Funneling	1.81 (1.43, 2.28)	2.68 (2.16, 3.32)	0.51 (0.31, 0.83)	0.63 (0.39, 1.00)	1.67 (1.22, 2.29)	2.26 (0.92, 5.54)
Wedging	3.56 (2.27, 5.59)	1.97 (1.21, 3.121)	1.63 (1.10, 2.43)	1.24 (0.68, 2.27)	3.29 (1.99, 5.42)	4.46 (1.68, 11.83)
Elastography	2.88 (1.88, 4.41)	1.59 (1.00, 2.54)	0.81 (0.44, 1.48)	1.70 (1.12, 2.57)	2.66 (1.65, 4.29)	3.61 (1.38, 9.46)
UCA	1.08 (0.84, 1.40)	0.59 (0.44, 0.82)	0.30 (0.18, 0.50)	0.38 (0.23, 0.61)	4.52 (3.57, 6.72)	1.36 (0.55, 3.34)
Volume	0.79 (0.33, 1.92)	0.44 (0.18, 1.08)	0.22 (0.09, 0.59)	0.28 (0.11, 0.73)	0.74 (0.29, 1.82)	6.13 (2.57, 14.62)

Note: Each diagonal cell (dark gray) contained the OR (95% CI) of each cervical assessment. Each off-diagonal cell (white) contained the relative OR (95% CI) between comparisons.

DISCUSSION & CONCLUSION

This is the first SRMA to assess the association between sonographic cervical assessments by adjusting the cut-off value instead of a diagnostic accuracy of the successful VD. Moreover, this study compared the association among different sonographic cervical assessments with successful VD using the relative OR. There was insufficient data to draw any conclusions on the main finding of the highest relative OR among all available sonographic cervical assessments with successful VD, especially in cervical volume (limited number of studies) which might be the cause of low precision. Cervical elastography which was included in the different types of measurements and software analyses showed low association with successful VD. For results that are more reliable and robust, additional studies on cervical volume and elastography may be required.

A strength of this study was that it considered the cut-off value of cervical assessments which might be the major heterogeneity, then used the adjustment of different cut-offs for pooling the association between the studies. Then this SRMA included a high number of studies in all languages. However, this study had several limitations. Firstly, the heterogeneity of protocols or methods of IOL. Secondly, the number of included studies in some sonographic cervical assessments were limited, which resulted in the low precision of the association, especially in the study on cervical volume, cervical wedging, and cervical elastography. Ongoing studies about these cervical assessments could be added on to yield more robust and more precise results.

Based on the evidence, among the six cervical assessments in terms of a higher association with success in VD, cervical volume, CL and UCA had the highest, second, and third ranks in the relative ORs for success VD. The results lead to the conclusion that obstetricians might be able to select the highest association of pre-induction sonographic cervical assessments with success in VD in pregnant women in clinical practice in terms of increasing success and reducing failure of IOL. This study should be developed further when more studies of cervical volume and novel sonographic cervical assessments with successful IOL are published.

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