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Can prophylactic transvaginal cervical cerclage improve pregnancy outcome in patients receiving cervical conization? A meta-analysis

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ABSTRACT

Objectives: Cervical conization could increase the risk of cervical insufficiency. This study systematically evaluated the value of prophylactic transvaginal cervical cerclage following cervical conization with regards to pregnancy outcome.

Material and methods: We performed a systematic review of the literature, using Web of Science, and Embase, the published time ranged from the date that database established to December 2019. Pregnant patients, who had a previous history of cervical conization for CIN or early cervical cancer, were enrolled. Two researchers searched these databases and estimated the included studies' quality independently, depending on the same criteria.

Results: Our meta-analysis is incorporate 3560 cases eventually. Meta-analysis showed that when compared to the no-cerclage group, the risk ratio (RR) of preterm birth in the prophylactic transvaginal cervical cerclage group was 1.85 [95% confidence interval (CI): 1.22–2.80; p = 0.004]; the RR of premature rupture of membranes was 1.5 (95% CI: 1.17–1.93; p = 0.001).

Conclusions: The rates of preterm birth were significantly higher in women following cervical conization with transvaginal cerclage than those without cerclage.

Key words: cervical conization; prophylactic cervical cerclage; preterm birth; premature rupture of membranes

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INTRODUCTION

The diagnosis rate of cervical intraepithelial neoplasia (CIN) and micro-invasive cervical carcinoma is much higher in recent years because of the wide usage of cervical sampling [1]. In addition, as delayed childbearing becomes a global trend, the proportion of women of reproductive age who are diagnosed with CIN, and early cervical cancer, is gradually increasing.

High grade CIN and micro-invasive cervical carcinoma can be treated with excisional procedures, also referred to as conization. These procedures include cold knife conization, the loop electrosurgical excision procedure (LEEP), and laser conization. The aim of these procedures is to remove a segment of the cervix for histological examination. The women of reproductive age who experienced these treatments may face negative fertility and pregnancy outcomes in the future.

It is currently considered that cervical conization may increase the risk of cervical insufficiency [2]. Some recent studies have revealed that previous cervical conization is associated with an increased risk of second-trimester pregnancy loss [3, 4], preterm premature rupture of membranes (PPROM), preterm delivery, and perinatal mortality.

A prospective series of research previously revealed that the detection of a short cervix (< 25 mm) on second-trimester transvaginal ultrasound examination was predictive of an increased risk of preterm birth in women who had experienced conization previously [5, 6]. It is generally accepted that cervical conization may increase the risk of cervical insufficiency; the role of prophylactic cervical cerclage has not been fully studied in women who have undergone previous cervical conization. The effectiveness of prophylactic transvaginal cervical cerclage remains controversial, and its use is associated with perinatal risks. Therefore, this study used the meta-analysis method to systematically evaluate the value of prophylactic transvaginal cervical cerclage following cervical conization in pregnant outcome, in order to provide evidence-based medical evidence for clinical treatment.

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MATERIALS AND METHODS

Information retrieval

We searched the database (Web of Science and Embase), setting the published time range from the date that database established to December 2019. The topic term words or free-searching term words used in the database included: cervical conization, co ld knife conization, CKC, loop electrosurgical excision, LEEP, and cervical cerclage.

Inclusion and exclusion criteria

Inclusion criteria

There were three types of inclusion criteria — 1. study type: studies were included in our meta-analysis if they represented a prospective or retrospective and were written in English; 2. research target: patients giving birth after cervical conization, those who received transvaginal cervical cerclage represented the case group, while those who did not receive cerclage represented the control group; 3. outcome index: studies were included in our meta-analysis if they reported the risk of preterm birth, premature rupture of membranes (PROM), preterm premature rupture of membranes (PPROM), perinatal mortality, or low birth weight.

Exclusion criteria

Studies were excluded if they were conference papers, reviews, lectures, or abstracts. Studies were also excluded if the full text was not available, or if they did not include the detailed information or enough data. Self-control clinical trials were also excluded, as were studies that included outcomes for twins, or higher-order multiple births; this was because of the association between plurality and preterm birth.

Quality evaluation

Cochrane risk of bias tool was used to evaluate the quality of incision articles. There were two researchers who searched these databases, estimated the included studies' quality independently, depending on the same criteria. In order to do this, the researchers used self-made data extraction forms, which targeted information relating to patient characteristics, the number of samples, obstetric outcomes, and neonatal outcomes. Subgroup analyses were only performed for cases involving preterm birth at < 34 weeks, and 34–36 + 6 weeks of gestation.

Statistical analysis

Meta-analysis was carried out using Review Manager 5.3 software. Our meta-analysis used both fixed-effects and random-effects depending on the heterogeneity. Statistical heterogeneity of results featured in the selected studies was assessed using the chi-squared test, expressed with the I2 index or p-value; when $p > 0.10$ or $I2 \leq 50\%$, we considered that there was no obvious heterogeneity in the included studies, and the fixed-effect model was used. When heterogeneity was detected, we made intensive efforts to identify a possible explanation. If a reasonable cause was found, then subgroup analysis was performed. Otherwise, a random-effects model was used. Variables are represented by relative risks (RRs); interval estimates are all based on 95% confidence intervals (95% CIs). Differences were considered to be statistically significant when $p < 0.05$.

RESULTS

Information retrieval

After first-circle database searching, 261 articles were detected. Following reading and screening, we accepted nine studies to be included in our final meta-analysis [7–15]. Figure 1 illustrated the literature screening process.

Basic characteristics and literature quality

Table 1 and Table 2 demonstrated the basic characteristics of studies included and Figure 2 showed the literature quality. Ultimately, nine studies were included in the final meta-analysis, featuring a total of 3560 patients; 605 women were treated by prophylactic transvaginal cervical cerclage following conization, while 2,955 women were not.

Systematic review

A risk ratio forest plot showed that the total risk ratio. The total risk ratio for preterm birth was 1.85 ($p = 0.004$),

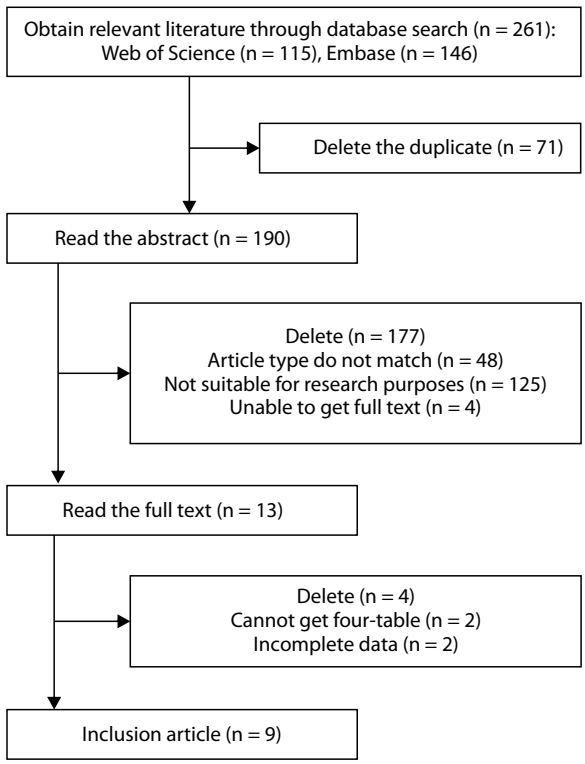


Figure 1. Document screening process and results

Table 1. Basic characteristics of the studies included in this meta-analysis

Study	Year	Nation	Study design	Transvaginal prophylactic cerclage specific method	Maternal age (mean)
Geum Joon Cho	2018	Korea	Retrospective	not clear	30.70
Harald Zeisler	1997	Austria	Retrospective	not clear	30.5 (22–41)
Ka Hyun Nam	2010	Korea	Retrospective	not clear	31 ± 3.7
Kei Miyakoshi	2019	Japan	Retrospective	not clear	33.80
Lindsay M. Kindinger	2016	Mexico	Retrospective	Monofilament/Braided cerclages	33.22
Minling Wei	2018	China	Retrospective	Transvaginal cervicoisthmic cerclage	29.9 ± 3.6
Mi-Young Shin	2010	Korea	Retrospective	not clear	32 (28–40)
Sharon Armarni	2011	Israel	Retrospective	not clear	32.22 ± 4.58
Tal Rafaeli-Yehudai	2014	Israel	Retrospective	Mcdonald and Shirodkar cerclage	32.80

while I2 was 71%. The total risk ratio of PROM was 1.5 (p = 0.001), with an I2 value of 47%. The total risk ratio of PPROM was 1.18 (p = 0.52), with an I2 value of 52%.

The results of our meta-analysis are shown in Figures 3–7. The use of prophylactic transvaginal cervical cerclage in women with cervical conization was associated with a significantly higher risk of preterm birth < 37 weeks (RR, 1.85; 95% CI, 1.22–2.80), 34–36 + 6 weeks (RR, 2.75; 95% CI, 1.69–4.47) and < 34 weeks (RR, 3.03; 95% CI, 1.06–8.67), and PROM (RR,1.5; 95% CI, 1.17–1.93).

Prophylactic transvaginal cervical cerclage, either with and without cerclage, was not significantly associated with the risk of PPROM (RR, 1.18; 95% CI,0.71–1.96), low birth weight (RR, 0.63; 95% CI, 0.24–1.67), or perinatal mortality (RR, m1.14; 95% CI,0.23–5.63).

Evaluation of publication evaluation

Funnel plot test results showed that there was no publication bias for preterm birth, PROM, PPROM, low birth weight, and perinatal mortality (Fig. 8).

DISCUSSION

Cervical conization is a standard treatment for women with high-grade CIN and micro-invasive carcinoma (Stage 1a1) [16–18]. Women with cervical dysplasia are at an increased baseline risk of preterm birth, and surgical excision confers additional risk [19, 20]. Pregnant patients, with a history of surgical excision, should therefore be considered as having high risk pregnancies [20]. Currently, more studies have found that conization therapy may have adverse effect on the following pregnancy outcomes, including preterm delivery, perinatal death and lower birth weight [3]. There are several factors that may underline these associations. First, the removal or destruction of a large portion of the collagen that makes up the cervical stromal may reduce tensile strength, thus reducing the mechanical competence of the cervix [21], and ultimately leading to premature dilation of the cervix during pregnancy. Second, excision of tissue and the absence of cervical glands may increase the risk of ascending infection. Third, cervical shortening causes bacteria to enter the uterine cavity from the vagina, thus promoting the migration of bacteria.

In order to prolong pregnancy, surgery remains the mainstay form of therapy. Cervical cerclage is a common method [22]; this method aims to provide mechanical support to the cervix and thereby reduce the risk of preterm birth, thus prolonging the period of gestation in pregnant women with cervical insufficiency [23, 24]. This procedure was initially described as a purse string suture around the cervix, performed using a vaginal approach. Some studies have indicated that cervical cerclage reduces the risk of preterm birth in women at high risk of preterm birth, and probably reduces the risk of perinatal deaths; furthermore, existing data appear to suggest that this method is more or less effective than other preventative treatments, particularly vaginal progesterone [25]. However, this method can lead to some adverse outcomes [26], including membrane rupture, chorioamnionitis, cervical lacerations, and suture displacement [27]. The incidence of complications varies widely with regards to the timing and indications for cerclage [28]. Overall, there is a low risk of complications with prophylactic cervical cerclage. Some studies have reported that cervical cerclage may increase the risk of preterm birth in women with a cervical length < 25 mm on ultrasound [29]. There is no consensus on the effect of cervical cerclage on pregnancy outcome following cervical conization. Therefore, in the present study, a systematic review discovered the advantage of prophylactic transvaginal cervical cerclage on pregnant outcome following cervical conization.

A transabdominal cerclage is used as an alternative for women for whom a transvaginal cerclage fails, or for women who have had large portions of their cervix removed during the treatment of oncological conditions [30]. This meta-anal-

Table 2. Outcomes of the studies included in this meta-analysis

Study	Geum Joon Cho		Harald Zeisler		Ka Hyun Nam		Kei Miyakoshi		Lindsay M. Kindinger		Minling Wei		MiYoung Shin		Sharon Armarnik		Tal Rafaeli-Yehudai	
Outcome/number	**with cerclage 161**	**without cerclage 914**	**with cerclage 30**	**without cerclage 39**	**with cerclage 6**	**without cerclage 59**	**with cerclage 171**	**without cerclage 1163**	**with cerclage 98**	**without cerclage 627**	**with cerclage 74**	**without cerclage**	**with cerclage 25**	**without cerclage 31**	**with cerclage 18**	**without cerclage 35**	**with cerclage 22**	**without cerclage 87**
Preterm labor (weeks)	17	39	7	8	3	15	49	281	24	46	16	/	9	9	7	5	/	/
34 ~ 36 + 6	/	/	/	/	/	/	/	/	18	38	8	/	4	3	/	/	/	/
< 3 4	/	/	/	/	/	/	/	/	6	8	8	/	5	6	/	/	7	5
miscarriage/delivery 20 ~ 27 + 6 weeks	/	/	/	/	/	/	/	/	/	/	5	/	2	2	/	/	/	/
preterm rupture of membranes (≥ 37 weeks)	/	/	4	6	/	/	15	82	/	/	/	/	/	/	/	/	3	17
preterm premature rupture of membranes (weeks)																		
< 37	10	22	/	/	/	/	22	155	/	/	/	/	10	13	2	6	/	/
< 34	/	/	/	/	/	/	/	/	/	/	/	/	5	7	/	/	/	/
< 28	/	/	/	/	/	/	/	/	/	/	/	/	2	2	/	/	/	/
Cesarean delivery	63	185	/	/	/	/	/	/	/	/	55	/	16	13	/	/	6	20
Apgar score 7 at 1 min	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	1	8
Perinatal mortality	/	/	/	/	/	/	/	/	/	/	/	/	0	0	1	2	1	3
Low birth weight Low birth weight	/	/	/	/	/	/	/	/	/	/	/	/	3	6	2	6	/	/
Birth weight (g) mean STD	/	/	3100 (706– –4150)	3044 (1150– –4500)	/	/	/	/	621– –4340	1450– –5074	/	/	3,000 (680– –4,200)	3,000 (1,220– –3,700)	2,984.67 ± 754.45	2,982.54 ± 830.26	2928.95 ± 878.71	2974.80 ± 719.73

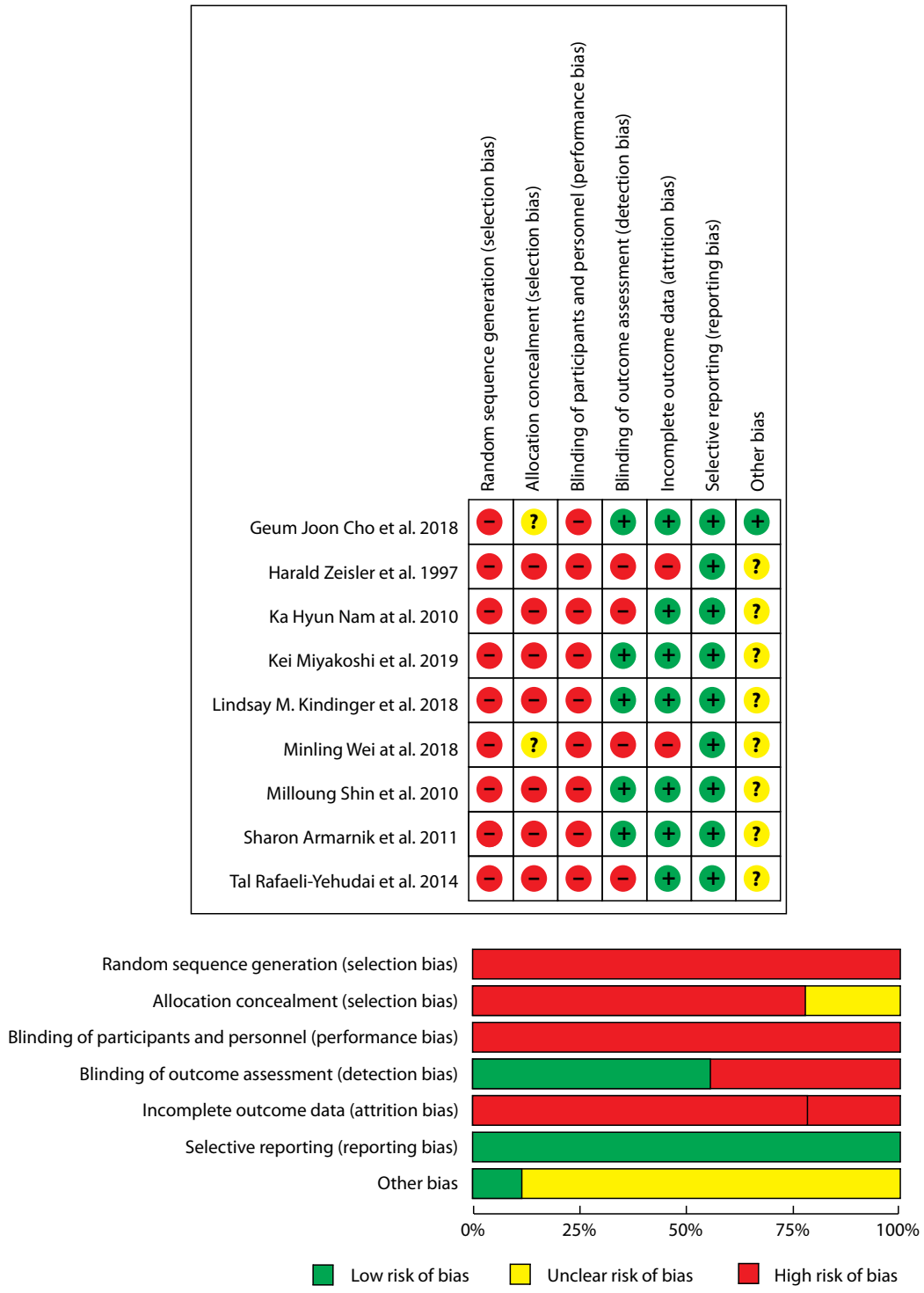
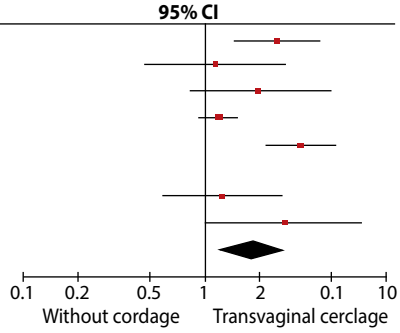


Figure 2. The risk of bias about the inclusion studies

ysis did not include publications relating to transabdominal cervical cerclage. There were two reasons for this. Firstly, when searching the literature, we only retrieved some case reports relating to transabdominal cervical cerclage after cervical conization [31–34]. Secondly, the indication for prophylactic cerclage through the abdomen is slightly different from that of transvaginal cerclage. Patients with cervical weakness who have an extremely short, deformed, or scarred cervix, cannot be adequately managed by prophylactic transvaginal cerclage [35]. There is a difference in the probability of adverse pregnancy outcomes when compared between patients who received transabdominal cerclage, and patients who received cerclage [36]. We retrieved four case reports; the characteristics of these cases are shown in Table 3.

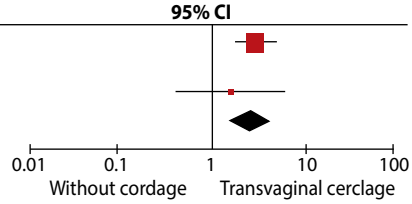
Study or subgroup	Transvaginal cerclage		Without cerclage			Ratio Risk	Ratio Risk
	Events	Total	Events	Total	Weight	M-H. Random, 95% CI	M-H. Random, 95% CI
Geum Joon Cho et al. 2018	17	161	39	914	16.4%	2.47 [1.44, 4.27]	
Harald Zeisler et al. 1997	7	30	8	39	11.0%	1.14 [0.46, 2.79]	
Ka Hyun Nam et al. 2010	3	6	15	59	10.8%	1.97 [0.79, 4.89]	
Kei Miyakoshi et al. 2019	49	171	281	1163	21.0%	1.19 [0.92, 1.53]	
Lindsay M. Kindinger et al. 2016	24	98	46	627	18.1%	3.34 [2.14, 5.21]	
Minting Wei et al. 2018	16	74	0	0		Not estimable	
MiYoung Shin et al. 2010	9	25	9	31	12.9%	1.24 [0.58, 2.65]	
Sharon Armarnik at al. 2011	7	18	5	35	9.8%	2.72 [1.00, 7.38]	
Total (95% CI)		583		2868	100.0%	1.85 [1.22, 2.80]	
Total events	132		403				

Heterogeneity: $Tau^2 = 0.19$; $Chi^2 = 20.40$, df = 6 (p = 0.002); $I^2 = 71\%$
Test for overall effect: Z = 2.92 (p = 0.004)
< 37 weeks



Study or subgroup	Transvaginal cerclage		Without cerclage			Ratio Risk	Ratio Risk
	Events	Total	Events	Total	Weight	M-H. Random, 95% CI	M-H. Random, 95% CI
Lindsay M. Kindinger et al. 2016	18	98	38	627	79.3%	3.03 [1.80, 5.09]	
Minting Wei et al. 2018	8	74	0	0		Not estimable	
MiYoung Shin et al. 2010	4	25	3	31	20.7%	1.65 [0.41, 6.71]	
Total (95% CI)		197		658	100.0%	2.75 [1.69, 4.47]	
Total events	30		41				

Heterogeneity: $Chi^2 = 0.64$, df =1 (p = 0.42); $I^2 = 0\%$
Test for overall effect: Z = 4.06 (p < 0.0001)
34–36 ± 6 weeks



Study or subgroup	Transvaginal cerclage		Without cerclage			Ratio Risk	Ratio Risk
	Events	Total	Events	Total	Weight	M-H. Random, 95% CI	M-H. Random, 95% CI
Lindsay M. Kindinger et al. 2016	6	98	8	627	33.6%	4.80 [1.70, 13.53]	
Minting Wei et al. 2018	8	74	0	0		Not estimable	
MiYoung Shin et al. 2010	5	25	6	31	33.0%	1.03 [0.36, 2.99]	
Tal Rafaeli-Yehudai et al. 2014	7	22	5	87	33.4%	5.54 [1.94, 15.79]	
Total (95% CI)		219		745	100.0%	3.03 [1.06, 8.67]	
Total events	26		19				

Heterogeneity: $Tau^2 = 0.58$; $Chi^2 = 6.01$, df = 2 (p = 0.05); $I^2 = 67\%$
Test for overall effect: Z = 2.07 (p < 0.04)
< 34 weeks

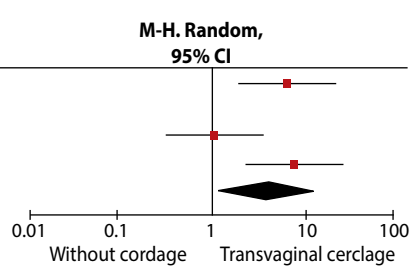


Figure 3. Meta-analysis of preterm birth

We consider that prophylactic transabdominal cerclage is an important treatment modality to improve obstetric prognosis and prevent unexpected complications for those with a history of transvaginal cervical cerclage failure, or multiple cervical cerclage operations. It is likely that the importance of transabdominal cerclage will increase with the development of conservative operations for invasive uterine cervical cancer. In addition, Ioannis Kyvernitakis previously reported that the results of transabdominal cerclage were comparable to those in singleton pregnancies, and that indications for transabdominal cerclage may be justifiable even in multiple gestations [33]. There is only a limited amount of data relating to prophylactic transabdominal cervical cerclage following cervical conization; further studies are now needed with larger sample sizes.

In order to avoid the significant levels of heterogeneity among different publications relating to pregnancy outcomes, we selected publications for our analysis_using strict criteria. The results were calculated by fixed models due to slight heterogeneity. The results of our meta-analysis showed that there was a large variation between the two groups with regards to the occurrence of preterm birth and PROM. The rates of preterm birth and PROM were significantly higher in women with prophylactic transvaginal cervical cerclage than those without cerclage. However, there was no significant difference in

Study or subgroup	With cerclage		Without cerclage			Ratio Risk	Ratio Risk
	Events	Total	Events	Total	Weight	M-H. Random, 95% CI	M-H. Random, 95% CI
Geum Joon Cho et al. 2018	10	161	22	914	9.5%	[1.25, 5.35]	
Harald Zeisler et al. 1997	4	30	6	39	7.5%	[0.27, 2.80]	
Kei Miyakoshi et al. 2019	37	171	137	1163	50.6%	[1.33, 2.54]	
MiYoung Shin et al. 2010	10	25	13	31	16.7%	[0.51, 1.80]	
Sharon Armarnik et al. 2011	2	18	6	35	5.9%	[0.15, 2.89]	
Tal Rafaeli-Yehudai et al. 2014	3	22	17	87	9.9%	[0.22, 2.17]	
Total (95% CI)		427		2269	100.0%	[1.17, 1.93]	
Total events	66		201				

Heterogeneity: $Chi^2 = 9.36$, df = 5 (p = 0.10); $I^2 = 47\%$
Test for overall effect: Z = 3.22 (p = 0.001)

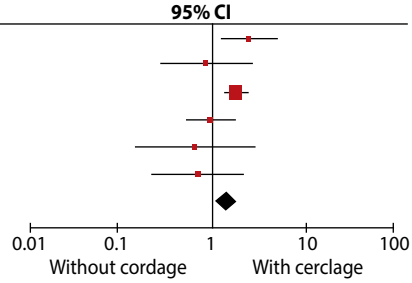


Figure 4. Meta-analysis of premature rupture of membranes (PROM)

Study or subgroup	With cerclage		Without cerclage			Ratio Risk	Ratio Risk
	Events	Total	Events	Total	Weight	M-H. Random, 95% CI	M-H. Random, 95% CI
Geum Joon Cho et al. 2018	10	161	22	914	24.7%	2.58 [1.25, 5.35]	
Kei Miyakoshi et al. 2019	22	171	155	1163	37.7%	0.97 [0.64, 1.46]	
MiYoung Shin et al. 2010	10	25	13	31	28.2%	0.95 [0.51, 1.80]	
Sharon Armarnik et al. 2011	2	18	6	35	9.3%	0.65 [0.15, 2.89]	
Total (95% CI)		375		2143	100.0%	1.18 [0.71, 1.96]	
Total events	44		196				

Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 6.30$, df = 3 (p = 0.10); $I^2 = 52\%$
Test for overall effect: Z = 0.65 (p = 0.52)

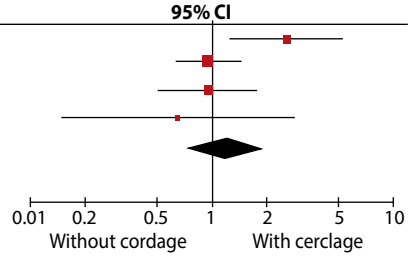


Figure 5. Meta-analysis of preterm premature rupture of membranes (PPROM)

Study or subgroup	With cerclage		Without cerclage			Ratio Risk	Ratio Risk
	Events	Total	Events	Total	Weight	M-H. Random, 95% CI	M-H. Random, 95% CI
MiYoung Shin et al. 2010	3	25	6	31	56.8%	0.62 [0.17, 2.23]	
Sharon Armarnik et al. 2011	2	18	6	35	43.2%	0.65 [0.15, 2.89]	
Total (95% CI)		43		66	100.0%	0.63 [0.24, 1.67]	
Total events	5		12				

Heterogeneity: $Chi^2 = 0.00$, df = 1 (p = 0.96); $I^2 = 0\%$
Test for overall effect: Z = 0.92 (p = 0.36)

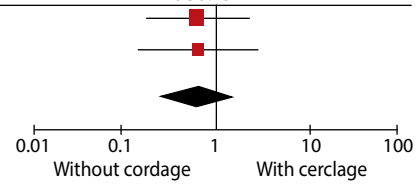


Figure 6. Meta-analysis of low birth weight

Study or subgroup	With cerclage		Without cerclage			Ratio Risk	Ratio Risk
	Events	Total	Events	Total	Weight	M-H. Random, 95% CI	M-H. Random, 95% CI
Sharon Armarnik et al. 2011	1	18	2	35	52.9%	0.97 [0.09, 10.01]	
Tal Rafaeli-Yehudai et al. 2014	1	22	3	87	47.1%	1.32 [0.14, 12.07]	
Total (95% CI)		40		122	100.0%	1.14 [0.23, 5.63]	
Total events	2		5				

Heterogeneity: $Chi^2 = 0.03$, df = 1 (p = 0.85); $I^2 = 0\%$
Test for overall effect: Z = 0.16 (p = 0.88)

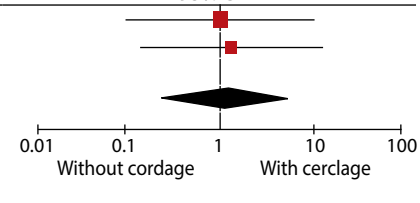


Figure 7. Meta-analysis of perinatal mortality

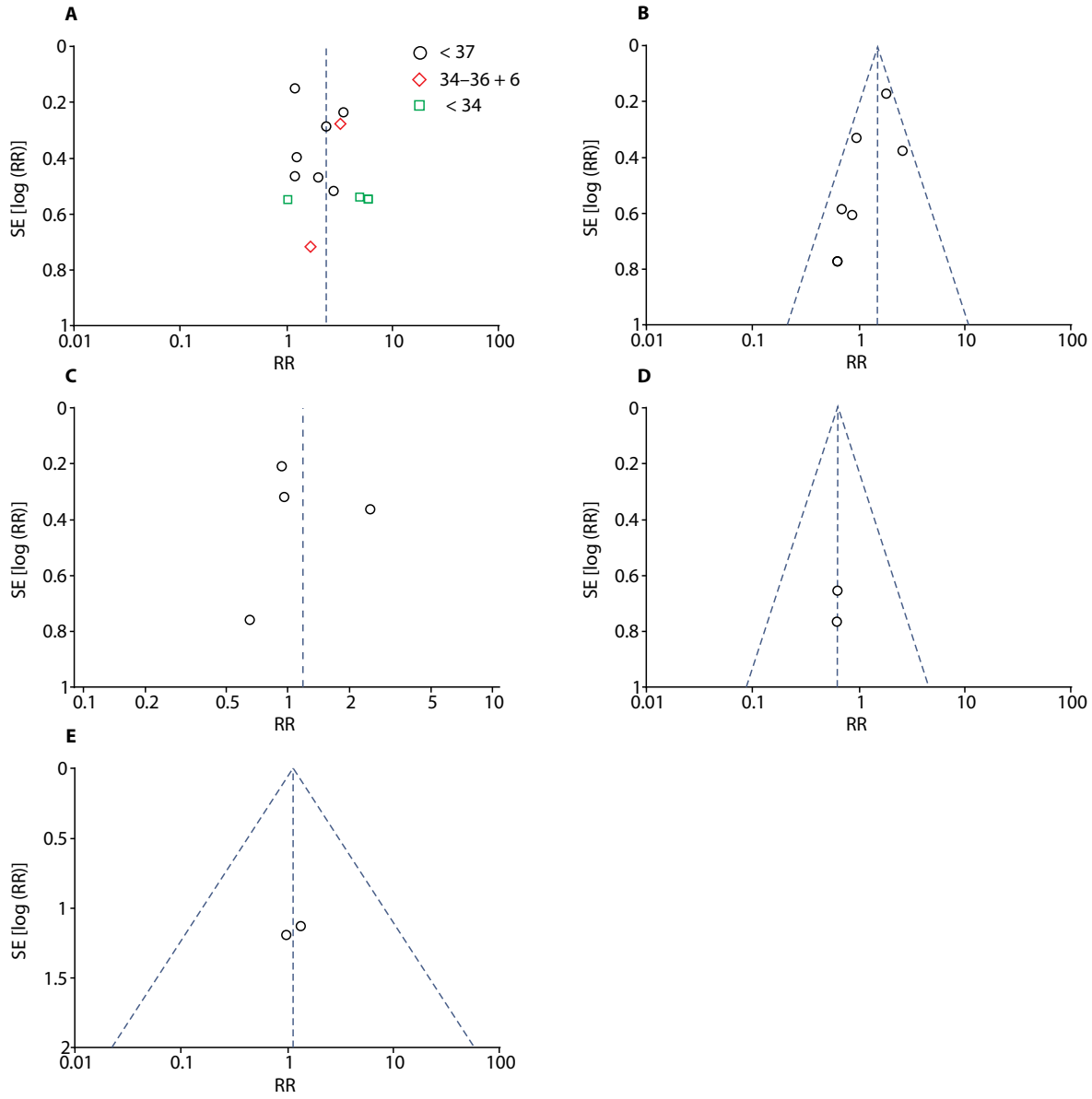


Figure 8. Funnel plot; A — preterm birth; B — PROM;C — PPROM; D — low birth weight; E — perinatal mortality

the risk of PPROM, low birth weight, and perinatal mortality, when compared between patients with prophylactic transvaginal cervical cerclage than those without cerclage. In most studies, the indication for cerclage operation was not stated in detail. Some of the heterogeneity between studies that we observed during our meta-analysis may have been associated with the different basic characteristic line, including pregnancy time, auxiliary exam level, medical history and whether there was a subjective judgment for cerclage.

This meta-analysis suggested that prophylactic transvaginal cerclage following conization increases the risk of preterm birth and PROM. In France, a history-indicated cerclage is not recommended for women with only a history of conization [31]. In another study, Kaye and Giraldo-Isaza considered that the increasing risk of PROM following cervical cerclage may related to the risk of ascending infection [32, 33].

Thus far, a variety of treatment methods has been used for cervical conization, including electrocautery, cryotherapy, laser ablation, cold knife conization, hot knife conization, and LEEP [36, 37]. Some studies reported that different conization methods have different effects on pregnancy outcomes [38, 39]. A recent meta -analysis reported that the risk of preterm birth and adverse sequelae in a subsequent pregnancy was increased after any local cervical treatments [40]. Furthermore, The larger the scope of the operation, the more obvious the adverse effect on the following preg-

Table 3. Characteristics of transabdominal cerclage

Study	Year	Nation	Case number	Conization method	Cerclage technique	pregnancy outcome	Neonatal outcome
Ioannis Kyvernitakis [33]	2014	Germany	15 (twins)	Radical Surgical Conization (15)	Transabdominal cervicoisthmic cerclage (14); Laparoscopic transabdominal cervicoisthmic cerclage (1)	Vaginal bleeding (1); Preterm labor (1); PPROM (1)	Alive (26); perinatal deaths (3); stillborn (1)
M. Besio [31]	2004	Chile	7 (singleton)	Wide conization (5); unknow (2)	Transabdominal cervicoisthmic cerclage	Chorioamnionitis (2, conization method unknow)	Stillborn (1)
Shinichi Ishioka [34]	2018	Japan	10 (singleton)	Conization twice (3), conization (2); radical Surgical Conization (5)	Transabdominal cerclage	Miscarriage (4); Second trimester of pregnancy (2); not conceive (1)	Not clear
Mads Riiskjaer [32]	2012	Denmark	11 (singleton)	Two or three previous conizations or a cervical amputation	Laparoscopic abdominal Cerclage	One woman delivered at 31 weeks, others had cesarean section at 36–39 weeks	Not clear

nancy outcomes [cold knife conization (CKC) > large loop excision of the transformation zone (LLETZ) > laser ablation (LA)], and was also higher for excision than ablation. The risk of preterm birth increased with the increasing conization depth [40].

The present meta-analysis includes the most recent literature. We used strict criteria, which could ensure the quality of the including published studies. We also calculated Newcastle-Ottawa-Scale NOS in order to determine the quality of the studies included. We also determined publication bias in order to ensure that our results were robust. For strengthening our conclusions, we also adopt meta-regression and in influence analyses.

There are some limitations in this meta-analysis that should be considered. First, the publications included were retrospective studies, and the overall quality of these studies was not high. Secondly, although we applied strict inclusion and exclusion criteria, it was possible that we did not include other biological factors that could have affected pregnancy outcome. Third, our analyses only considered publications that were written in English. Finally, we were not able to sub-divide the conization according to the height of the cervical conization column.

CONCLUSIONS

In conclusion, our meta-analysis suggested that prophylactic transvaginal cervical cerclage following conization increases the risk of preterm birth and PROM. Further studies, with a larger sample size, should now be performed in order to confirm our findings.

Conflicts of interest

The authors declare no conflict of interest.

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