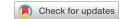
Early amniotomy after cervical ripening for induction of labor: a systematic review and metaanalysis of randomized controlled trials



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OBJECTIVE DATA: Timing of artificial rupture of membranes (ie, amniotomy) in induction of labor is controversial, because it has been associated not only with shorter labors, but also with fetal nonreassuring testing, at times necessitating cesarean delivery. The aim of this systematic review and metaanalysis of randomized trials was to evaluate the effectiveness of early amniotomy vs late amniotomy or spontaneous rupture of membranes after cervical ripening.

STUDY: The search was conducted with the use of electronic databases from inception of each database through February 2019. Review of articles included the abstracts of all references that were retrieved from the search.

STUDY APPRAISAL AND SYNTHESIS METHODS: Selection criteria included randomized clinical trials that compared early amniotomy vs control (ie, late amniotomy or spontaneous rupture of membranes) after cervical ripening with either Foley catheter or prostaglandins at any dose. The primary outcome was the incidence of cesarean delivery. The summary measures were reported as summary relative risk with 95% of confidence interval with the use of the random effects model of DerSimonian and Laird.

RESULTS: Four trials that included 1273 women who underwent cervical ripening with either Foley catheter or prostaglandins and then were assigned randomly to either early amniotomy, late amniotomy, or spontaneous rupture of membranes (control subjects) were included in the review. Women who were assigned randomly to early amniotomy had a similar risk of cesarean delivery (31.1% vs 30.9%; relative risk, 1.05; 95% confidence interval, 0.71-1.56) compared with control subjects and had a shorter interval from induction to delivery of approximately 5 hours (mean difference, -4.95 hours; 95% confidence interval, -8.12 to -1.78). Spontaneous vaginal delivery was also reduced in the early amniotomy group, but only 1 of the included trials reported this outcome (67.5% vs 69.1%; relative risk, 0.78; 95% confidence interval, 0.66—0.93). No between-group differences were reported in the other obstetrics or perinatal outcomes. **CONCLUSION:** After cervical ripening, routine early amniotomy does not increase the risk of cesarean delivery and reduces the interval from induction to delivery.

Key words: cesarean delivery, delivery, Foley catheter, induction of labor, prostaglandins

In United States, approximately 20% of all pregnant women receive induction of labor. 1,2 In the case of

unfavorable cervix, cervical ripening may be offered. Cervical ripening can be achieved with mechanical methods, such

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The authors report no conflict of interest.

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as Foley catheter, or pharmacologic methods, such as prostaglandins.^{1,3}

Amniotomy, or artificial rupture of membranes, can be performed during induction of labor, because it has been associated with the release of chemicals and hormones that stimulate contractions.4

Amniotomy may be performed during vaginal examination, is not painful, and does not require anesthesia.4 Major complications that are associated with this procedure include cord prolapse, ascending infections, fetal decelerations, and bleeding.4

Benefits of amniotomy may include shorter labors.4 Risks may include nonreassuring fetal testing, which in some cases may necessitate a cesarean delivery.4

When to perform amniotomy after cervical ripening for an induction of labor is still controversial.^{1,4} Indeed, amniotomy can be performed in an early stage, in a late stage, or one can wait for spontaneous rupture of membranes. Early amniotomy is defined as artificially rupture of membranes before the active phase of labor. Late amniotomy is defined as artificial rupture of membranes after the onset of active phase of labor.

The aim of this systematic review and metaanalysis of randomized controlled trials (RCTs) was to evaluate the effectiveness of early amniotomy vs late amniotomy or spontaneous rupture of membranes in women who received cervical ripening.

Materials and Methods

Search strategy

This review was performed according to a protocol that was recommended for systematic review.⁵ The search was conducted with the use of MEDLINE, EMBASE, Web of Sciences, Scopus, ClinicalTrial.gov, OVID, and Cochrane

AJOG at a Glance

Why was this study conducted?

The purpose of this study was to determine the impact of early amniotomy after cervical ripening on the risk of cesarean delivery.

Key findings

Women who were assigned randomly to early amniotomy had a similar risk of cesarean delivery (31.1% vs 30.9%; relative risk, 1.05; 95% confidence interval, 0.71-1.56) compared with control subjects (ie, late amniotomy or spontaneous rupture of membranes) and had shorter interval from induction to delivery of approximately 5 hours.

What does this add to what is known?

After cervical ripening, routine early amniotomy does not increase the risk of cesarean delivery and reduces the interval from induction to delivery.

Library as electronic databases from their inception until February 2019. Search terms that were used were "early amniotomy," "late amniotomy," "induction of labor," "cervical ripening," "Foley catheter," and "prostaglandins." No restrictions for language or geographic location were applied. We also used the reference lists of all identified articles to find additional studies.

Study selection

We identified all RCTs that compared early amniotomy (ie, intervention group) with late amniotomy or spontaneous rupture of membranes (ie, control group) in women who first underwent cervical ripening. Cervical ripening includes either mechanical (eg, Foley catheter) or pharmacologic (eg, prostaglandins) methods at any dose. Early amniotomy was defined as artificial rupture of the membranes soon after successful cervical ripening (eg, expulsion of Foley balloon or achievement of ≥3 cm cervical dilation or a Bishop score of ≥ 5). Late amniotomy was defined as artificial rupture of membranes after the onset of active phase of labor.

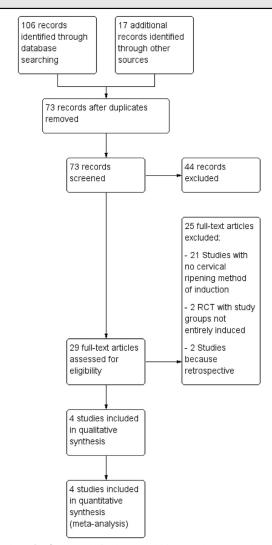
Types of participants included pregnant women at term with singleton gestation and cephalic presentation who were admitted for induction of labor because of different conditions.

Two authors (V.D.V., L.C.) independently assessed inclusion criteria, risk of bias, data extraction, and data analysis. Disagreement was resolved by discussion with a third reviewer (V.B.).

Risk of bias assessment

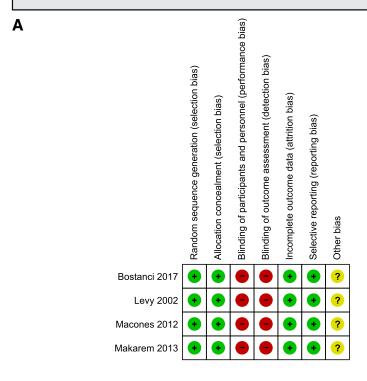
The risk of bias in each included study was assessed by with the use of the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions.5 Seven domains that are related to risk of bias were assessed in each included trial because there is evidence that these issues are associated with biased estimates of treatment effect: (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessment, (5) incomplete outcome data, (6) selective reporting, and (7) other bias. Review authors' judgments were

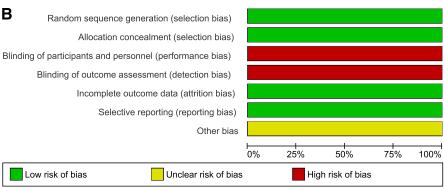
FIGURE 1 Flow diagram of studies identified in the systematic review



Preferred Reporting Item for Systematic Reviews and Meta-analyses template.







A, Summary of risk of bias for each trial. The plus sign indicates low risk of bias; the minus sign indicates high risk of bias; the question mark indicates unclear risk of bias. B, Risk of bias graph about each risk of bias item presented as percentages across all included studies.

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categorized as "low risk," "high risk," or "unclear risk" of bias. All analyses were done with the use of an intention-to-treat approach; the cases of the women were evaluated according to the treatment group to which they were randomly allocated in the original trials.

Primary and secondary outcomes

The primary outcome was the incidence of cesarean delivery. The secondary

outcomes were overall length of labor (defined as induction to delivery interval), latency from randomization or induction to delivery, vaginal delivery within 24 hours from randomization, mode of delivery, and neonatal outcomes, which included birthweight, Apgar scores, meconium-stained amniotic fluid, neonatal sepsis, need for resuscitation, and admission to the neonatal intensive care unit.

Statistical analysis

The data analysis was completed independently by 2 authors (V.D.V., L.C.) who used Review Manager (version 5.3; The Nordic Cochrane Centre, Cochrane Collaboration, 2014, Denmark). Copenhagen, completed analyses then were compared, and any difference was resolved by discussion with a third reviewer (G.S.). The summary measures were reported as summary relative risk (RR) or as weighted mean difference with 95% of confidence interval (CI) with the use of the random effects model of DerSimonian and Laird. I-squared (Higgins I²) was used to identify heterogeneity.

Data from each eligible study were extracted without modification of original data onto custom-made data collection forms. A 2×2 table was assessed for RR; for continuous outcomes means±standard deviation were extracted and imported into Review Manager.

A probability value of <.05 was considered statistically significant.

The metaanalysis was reported according to the Preferred Reporting Item for Systematic Reviews and Metaanalyses statement.6

Results

Study characteristics

Four trials that included 1273 women who underwent cervical ripening with either Foley catheter or prostaglandins and then were randomized to either early amniotomy, late, or spontaneous rupture of membranes were included in the metaanalysis (Figure 1).^{7–10}

The quality of the RCTs that were included in our metaanalysis was assessed with the use of the 7 criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions.⁵ All of the included studies had "low risk" of bias in "random sequence generation." Adequate methods for allocation of women and for random sequence generation were used in all the trials (Figure 2).

All the studies included singleton pregnancies with cephalic presentation at term or late preterm that had been

IABLE I				
Characteristics	of the	trials	that were	included

	Study									
Characteristic	Levy et al (2002) ⁷	Macones et al (2012) ⁸	Makarem et al (2013) ⁹	Bostanci et al (2017) ¹⁰						
Location	Israel	United States	Egypt	Turkey						
Type of cervical ripening	Foley inflated with 60 mL of sterile saline solution intracervically	Different methods (misoprostol or Foley bulb or both), at discretion of the treating physician	Misoprostol 50 $\mu \mathrm{g}$ vaginally, every 6 hr	Dinoprostone 10 mg vaginally						
Length of cervical ripening	Spontaneous expulsion of the Foley catheter or 24 hrs	Not reported	Until \geq 3 contractions of 40 sec duration occur over 10 min or when the maximum dose is reached (4 doses=200 μ g)	24 Hours or removed earlier if the patient has ≥3 contractions within 10 min, lasting 45 sec resulting in cervical change or longer, or dilation of 4 cm with any frequency of contractions						
Intervention group	Early amniotomy soon after removal or expulsion of the Foley catheter	Early amniotomy soon after cervical ripening	Early amniotomy soon after last dose of misoprostol administration	Early amniotomy soon after removal of the dinoprostone						
Timing of early amniotomy	After expulsion of Foley catheter	Cervical dilation ≤4 cm	Cervical dilation at 3 cm	Cervical dilation at 3 cm						
Control group	Late amniotomy defined as amniotomy when regular contractions and/or change in cervical dilation or effacement occurred	Late amniotomy defined as amniotomy with cervical dilation >4 cm	Spontaneous rupture of the membranes	Spontaneous rupture of the membranes						
Inclusion criteria	Singleton, \geq 38 weeks gestation, vertex presentation with intact membranes, cervical dilation of \leq 1 cm, and no regular contractions		gestation, cephalic presentation, amniotic fluid index >5 cm,	Singleton, \geq 37 weeks gestation, cephalic presentation intact membranes, Bishop score $<$ 5						
Exclusion criteria	Previous uterine surgery, vaginal bleeding, high-risk pregnancies	HIV infection or cervical dilation of $>$ 4 cm at admission examination	Suspected macrosomia, intrauterine growth restriction, polyhydramnios	Category II or III fetal heart rate pattern, fetal anomalies, fetal death						
Timing of randomization	After expulsion of Foley catheter	At the time of cervical ripening	At the time of cervical ripening	At the time of cervical ripening						
Sample size ^a	168 (80 vs 88)	585 (292 vs 293)	320 (160 vs 160)	200 (100 vs 100)						
Primary outcome	Cesarean delivery	Time from randomization to delivery; delivery within 24 hr from random assignment	Vaginal delivery within 24 hr from random assignment	Delivery within 24 hr from random assignment						

^a Data are presented as total number (number in the intervention vs number in the control group).

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TABLE 2
Characteristics of the women whose cases were included

	Study				
Characteristic	Levy et al (2002) ⁷	Macones et al (2012) ⁸	Makarem et al (2013) ⁹	Bostanci et al (2017) ¹⁰	Total
Maternal age, y ^a	28±6 vs 28±5.6	22.7±5.8 vs 23.3±6.2	23.9±4.2 vs 24.3±4.2	28.0±5.9 vs 27.6±6.4	
Body mass index, kg/m ^{2a}	Not reported	28±4.2 vs 28±3.9	Not reported	29.4±4.9 vs 29.4±4.8	_
Nulliparous, n/N (%)	32/80 (40.0) vs 37/88 (42.0)	292/292 (100) vs 293/293 (100)	Not reported	57/100 (57.0) vs 54/100 (54.0)	381/472 (80.7) vs 384/481 (79.8)
Multiparous, n/N (%)	48/80 (60.0) vs 51/88 (57.9)	0/292 vs 0/293	Not reported	43/100 (43.0) vs 46/100 (46.0)	91/472 (19.3) vs 97/481 (20.1)
Gestational age at randomization, wk ^a	41±1.1 vs 41±1	$39.7{\pm}1.4$ vs $39.5{\pm}1.4$	40±4.1 vs 40.7±4.9	$39.9{\pm}1.4$ vs $39.8{\pm}1.4$	_
Group B streptococcus carrier, n/N (%)	Not reported	85/292 (29.1) vs 88/293 (30.0)	Not reported	Not reported	85/292 (29.1) vs 88/293 (30.0)
Indication for induction					
After due date, n/N (%)	35/80 (43.7) vs 42/88 (47.7)	117/292 (40.0) vs 114/293 (38.9)	126/160 (78.8) vs 132/160 (82.5)	66/100 (66.0) vs 70/100 (70.0)	344/632 (54.4) vs 358/641 (55.8)
Oligohydramnios	17/80 (21.3) vs 23/88 (26.2)	Not reported	Not reported	9/100 (9.0) vs 7/100 (7.0)	26/180 (14.4) vs 30/188 (15.9)
Pregnancy-induced hypertension/mild preeclampsia, n/N (%)	25/80 (31.3) vs 19/88 (21.5)	85/292 (29.1) vs 79/293 (26.9)	34/160 (21.3) vs 28/160 (17.5)	9/100 (9.0) vs 7/100 (7.0)	153/632 (24.2) vs 133/641 (20.7)
Chronic hypertension, n/N (%)	Not reported	Not reported	Not reported	0/100 vs 1/100 (1.0)	0/100 vs 1/100 (1.0)
Bad obstetric history, n/N (%)	3/80 (3.7) vs 4/88 (4.6)	Not reported	Not reported	Not reported	3/80 (3.7) vs 4/88 (4.6)
Gestational diabetes mellitus, n/N (%)	Not reported	Not reported	Not reported	6/100 (6.0) vs 5/100 (5.0)	6/100 (6.0) vs 5/100 (5.0)
Cholestasis, n/N (%)	Not reported	Not reported	Not reported	10/100 (10.0) vs 10/100 (10.0)	10/100 (10.0) vs 10/100 (10.0)
Fetal growth restriction, n/N (%)	Not reported	17/292 (5.8) vs 21/293 (7.1)	Not reported	Not reported	17/292 (5.8) vs 21/293 (7.1)
Epidural rate, n/N (%)	62/80 (77.5) vs 60/88 (68.2)	269/292 (92.1) vs 275/293 (93.8)	Not reported	Not reported	331/372 (88.9) vs 335/381 (87.9)

 $^{^{\}rm a}$ Data are presented as mean $\pm {\rm standard}$ deviation.

FIGURE 3 Forest plot for the risk of cesarean delivery

	Early amnie	otomy	Contr	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	I M-H, Random, 95% CI
Bostanci 2017	14	100	19	100	19.5%	0.74 [0.39, 1.39]	
Levy 2002	20	80	7	88	14.9%	3.14 [1.40, 7.03]	_
Macones 2012	120	292	117	293	35.3%	1.03 [0.85, 1.25]	•
Makarem 2013	43	160	55	160	30.4%	0.78 [0.56, 1.09]	
Total (95% CI)		632		641	100.0%	1.05 [0.71, 1.56]	*
Total events	197		198				
Heterogeneity: Tau ² =	0.11; Chi ² = 1	0.85, df =	= 3 (P = 0)				
Test for overall effect:	Z = 0.23 (P =	0.82)					0.01 0.1 1 10 100 Favours [Early amniotomy] Favours [Control]

Cl. confidence interval: df. degrees of freedom: M-H. Mantel-Haenszel.

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admitted for induction of labor for various reasons (Tables 1 and 2). All women received cervical ripening with either Foley catheter or prostaglandins and then were assigned randomly to either early amniotomy (ie, amniotomy soon after cervical ripening) or control group. Control group in 2 trials included spontaneous rupture of membranes and in 2 trials was defined as late amniotomy (ie, amniotomy performed at >4 cm or when regular contractions and/or change in cervical dilation or effacement occurred; Table 1).

All trials, but 1,⁷ randomly assigned women at the time of cervical ripening. Levy et al⁷ randomly assigned women after cervical ripening (ie, after catheter expulsion).

Synthesis of results

Women who were randomly assigned to the early amniotomy group had similar risk of cesarean delivery compared with control subjects (31.1% vs 30.9%; RR,

1.05; 95% CI, 0.71-1.56; Figure 3). Spontaneous vaginal delivery was reduced in the early amniotomy group, but only 1 of the included trials reported this outcome (67.5% vs 69.1%; RR, 0.78; 95% CI, 0.66-0.93).

Randomization to delivery interval was reported only by Levy et al⁷; the other 3 trials reported data on latency from induction (either cervical ripening or induction of labor) to delivery. Women who were assigned randomly to the early amniotomy group had a shorter interval from induction to delivery of approximately 5 hours (weighted mean difference, −4.95 hours; 95% CI, −8.12 to -1.78; Figure 4; Table 3).

No between-group differences were reported in the other obstetrics or perinatal outcomes (Tables 3-5).

Comment

Main findings

This metaanalysis from 4 RCTs evaluated the effect on cesarean delivery rate of early amniotomy soon after cervical ripening in women with singleton gestations and cephalic presentation at term. Pooled results showed that early amniotomy was not associated with an increased risk of cesarean delivery and was associated with shorter interval from induction to delivery of approximately 5 hours. The reduction in spontaneous vaginal delivery was based on a single study and therefore did not represent an actual result of the metaanalysis. Early amniotomy was not associated with any other maternal or perinatal benefits.

Our study has several strengths. The 4 trials that were included had a low risk of bias. Intention-to-treat analysis was used. To the best of our knowledge, no previous metaanalysis on this issue has been performed. Findings of this metaanalysis were limited, however, by the small number of the included trials and included participants. Moreover, none of the trials stratified data by parity, and only Macones et al⁸ included only

FIGURE 4			
Forest plot for	induction to	delivery	interval

Early amniotomy		С	ontro	Mean Difference			Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI Year	IV, Random, 95% CI		
Macones 2012	19	9.1	292	21.3	10.1	293	33.7%	-2.30 [-3.86, -0.74] 2012	-		
Makarem 2013	9.7	4.6	160	13.6	5.6	160	35.1%	-3.90 [-5.02, -2.78] 2013	=		
Bostanci 2017	13.7	7.4	100	22.7	8.4	100	31.2%	-9.00 [-11.19, -6.81] 2017	-		
Total (95% CI)			552			553	100.0%	-4.95 [-8.12, -1.78]	•		
0 ,	Heterogeneity: Tau² = 7.13; Chi² = 24.37, df = 2 (P < 0.00001); l² = 92% Test for overall effect: Z = 3.06 (P = 0.002) Test for overall effect: Z = 3.06 (P = 0.002) Test for overall effect: Z = 3.06 (P = 0.002)										

CI, confidence interval; df, degrees of freedom; M-H, Mantel-Haenszel.

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TABLE 3

Labor and delivery outcomes

	Study						Relative risk ^a or weighted
Outcome	Levy et al (2002) ⁷	Macones et al (2012) ⁸	Makarem et al (2013) ⁹	Bostanci et al (2017) ¹⁰	Total	l², %	mean difference ^b (percentages) [95% confidence interval]
Cesarean delivery, n/N (%)	20/80 (25.0) vs 7/88 (7.9)	120/292 (41.1) vs 117/293 (39.9)	43/160 (26.9) vs 55/160 (34.4)	14/100 (14.0) vs 19/100 (19.0)	197/632 (31.1) vs 198/641 (30.9)	72	1.05 [0.71—1.56]
Randomization to delivery interval, hr ^c	9.4±4.2 vs 7.9±3.1	Not reported	Not reported	Not reported	_	NA	1.50 (0.37-2.63) ^d
Starting induction to delivery interval, hr ^c	NA	19.0±9.1 vs 21.3±10.1	9.7±4.6 vs 13.6±5.6	13.7±7.4 vs 22.7±8.4	_	92	-4.95 (-8.12 to -1.78) ^d
Vaginal delivery, n/N (%)	60/80 (75.0) vs 81/88 (92.0)	172/292 (58.9) vs 176/293 (60.0)	117/160 (73.1) vs 105/160 (65.6)	86/100 (86.0) vs 81/100 (81.0)	435/632 (68.8) vs 443/641 (69.1)	73	0.99 [0.87—1.12]
Spontaneous vaginal delivery, n/N (%)	54/80 (67.5) vs 76/88 (86.4)	Not reported	Not reported	Not reported	54/80 (67.5) vs 76/88 (86.4)	NA	0.78 [0.66-0.93] ^d
Operative vaginal delivery, n/N (%)	6/80 (7.5) vs 5/88 (5.6)	Not reported	Not reported	Not reported	6/80 (7.5) vs 5/88 (5.6)	NA	1.32 [0.42-4.16]
Delivery within 24 hrs, n/N (%) ^e	Not reported	199/292 (68.1) vs 164/293 (55.9)	160/160 (100) vs 160/160 (100)	79/100 (91.9) vs 35/100 (43.2)	438/552 (79.3) vs 359/553 (64.9)	100	1.40 [0.29—6.65]
Vaginal delivery within 24 hrs, n/N (%) ^e	Not reported	Not reported	117/160 (73.1) vs 105/160 (65.6)	Not reported	117/160 (73.1) vs 105/160 (65.6)	NA	1.11 [0.96—1.29]
Cesarean delivery for arrested second stage of labor, n/N (%)	12/80 (15.0) vs 3/88 (3.3)	Not reported	18/160 (11.3) vs 22/160 (13.8)	5/100 (5.0) vs 4/100 (4.0)	35/340 (10.3) vs 29/348 (8.3)	67	1.50 [0.54—4.14]
Cesarean delivery for non-reassuring fetal heart rate tracing, n/N (%)	5/80 (6.2) vs 3/88 (3.4)	Not reported	16/160 (10) vs 21/160 (13.1)	6/100 (6) vs 5/100 (5)	27/340 (7.9) vs 29/348 (8.3)	0	0.93 [0.56—1.54]
NA not applicable							

NA, not applicable.

a Indicated with brackets; b Indicated with parentheses; c Data are presented as mean±standard deviation; d Statistically significant; Data from randomization.

TABLE 4 Neonatal outcomes	es						
	Study						Relative risk ^a or weighted
Outcome	Levy et al (2002) ⁷	Macones et al (2012) ⁸	Makarem et al (2013) ⁹	Bostanci et al (2017) ¹⁰	Total	۱², %	mean difference [55% confidence intervals]
Birthweight, g ^c	3311±382 vs 3272±444	3323±516 vs 3311±566	Not reported	3265.45±393.07 vs 3354.9±387.37	1	32	-0.03 [-0.19-0.14]
Birthweight > 4000 g, n/N (%)	3/80 (3.8) vs 2/88 (2.3)	Not reported	Not reported	Not reported	3/80 (3.8%) vs 2/88 (2.3%)	NA	1.65 [0.28—9.62]
Apgar at 1 min ^c	Not reported	Not reported	Not reported	7.9±0.7 vs 7.8±0.8	1	NA	0.13 [-0.15-0.41]
Apgar at 5 min ^c	Not reported	8.6 vs 8.6 ^d	Not reported	8.8±0.73 vs 8.9±0.5	1	NA	-0.03 [-0.31 -0.25]
Apgar <7 at 1 min, n/N (%)	0/80 vs 0/88	Not reported	16/160 (10.0) vs 19/160 (11.9)	Not reported	16/240 (6.6) vs 19/248 (7.6)	NA	0.84 [0.45—1.58]
Apgar <7 at 5 min, n/N (%)	0/80 vs 0/88	Not reported	8/160 (5.0) vs 15/160 (9.4)	Not reported	8/240 (3.3) vs 15/248 (6)	NA	0.53 [0.23—1.22]

l Indicated with brackets; ^b Indicated with parentheses; ^c Data are presented as mean±standard deviation; ^d Standard deviation not reported. Early anniotomy vs control in induction of labor after cervical ripening: a metaanalysis. Am J Obstet Gynecol 2020.

NA, not applicable.

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nulliparous women. Therefore, subgroup analyses according to parity were not feasible.

Regarding the complications of the amniotomy, no differences were reported in the rate of cord prolapse in the intervention or in the control group. However, this is a very rare outcome, with an overall rate of <1%. Therefore, the nonsignificant increased risk in cord prolapse and chorioamnionitis needs to be explored in larger studies.

Implications

A shorter length of labor with early induction is associated with perinatal benefits and higher maternal satisfaction. 11,12 Different techniques have been studied during labor for the improvement of obstetrics outcomes. 13-19 For example, level 1 data showed that discontinuation of oxytocin infusion after the active phase of labor at approximately 5 cm is reached reduces the risk of cesarean delivery and of uterine tachysystole compared with continuous oxytocin infusion. ¹⁶ A policy of intravenous fluids at a rate of 250 mL/hr rather than 125 mL/hr also has been associated with a shorter duration of labor. 15

Use of early amniotomy has also been proposed as a technique to reduce the length of labor, but concerns have been raised regarding the increased risk of cesarean delivery.4 Our review showed that, if this procedure is applied in women after they underwent cervical ripening, there was no increased risk of cesarean delivery and shortened interval from induction to delivery.

There are 5 Cochrane reviews that deal with amniotomy. 4,20-23 Bricker et al, 20 in a metaanalysis of 2 trials comprising 310 women, found that amniotomy alone compared with a single dose of vaginal prostaglandins for women with a favorable cervix led to an increased need for oxytocin augmentation in the amniotomy group. Howarth and Botha²¹ in their review that included 17 trials that involved 2566 women showed that amniotomy and intravenous oxytocin resulted in fewer women being undelivered vaginally at 24 hours than amniotomy alone. In secondary results, amniotomy and intravenous oxytocin resulted in significantly

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TABLE 5
Maternal and neonatal complications

	Study, n/N (%)						Relative risk
Complication	Levy et al (2002) ⁷	Macones et al (2012) ⁸	Makarem et al (2013) ⁹	Bostanci et al (2017) ¹⁰	Total	l², %	(95% confidence interval)
Chorioamnionitis	7/80 (8.7) vs 2/88 (2.3)	34/292 (11.5) vs 25/293 (8.5)	0/160 vs 0/160	5/100 (5.0) vs 4/100 (4.0)	46/632 (7.3) vs 31/641 (4.8)	0	1.47 (0.95—2.28)
Need for amnioinfusion	Not reported	55/292 (19) vs 56/293 (19)	Not reported	Not reported	55/292 (18.8) vs 56/293 (19.1)	NA	0.99 (0.71-1.38)
Cord prolapse	0/80 vs 0/88	2/292 (0.7) vs 0/293	0/160 vs 0/160	0/100 vs 0/100	2/632 (0.7) vs 0/641	NA	5.02 (0.24—104.05)
Postpartum hemorrhage	Not reported	24/292 (8.2) vs 30/293 (10.2)	Not reported	Not reported	24/292 (8.2) vs 30/293 (10.2)	NA	0.80 (0.48-1.34)
Placental abruption	Not reported	1/292 (0.3) vs 2/293 (0.6)	Not reported	Not reported	1/292 (0.3) vs 2/293 (0.6)	NA	0.50 (0.05-5.50)
Tachysystole	Not reported	Not reported	6/160 (3.8) vs 4/160 (2.5)	7/100 (7.0) vs 7/100 (7.0)	13/260 (5.0) vs 11/260 (4.2)	0	1.17 (0.54-2.57)
Nausea	Not reported	Not reported	35/160 (21.8) vs 29/160 (18.1)	28/100 (28.0) vs 20/100 (20.0)	63/260 (24.2) vs 49/260 (18.8)	0	1.29 (0.92—1.79)
Meconium-stained amniotic fluid	Not reported	Not reported	13/160 (8.1) vs 19/160 (11.9)	Not reported	13/160 (8.1) vs 19/160 (11.9)	NA	0.68 (0.35—1.34)
Neonatal sepsis	Not reported	28/292 (9.6) vs 33/293 (11.2)	Not reported	Not reported	28/292 (9.6) vs 33/293 (11.2)	NA	0.85 (0.53—1.37)
Need for neonatal resuscitation	Not reported	Not reported	13/160 (8.1) vs 19/160 (11.9)	6/100 (6.0) vs 6/100 (6.0)	19/260 (7.3) vs 25/260 (9.6)	0	0.76 (0.43—1.34)
Admission to the neonatal intensive care unit	Not reported	40/292 (13.6) vs 44/293 (15)	8/160 (5.0) vs 13/160 (8.1)	8/100 (8.0) vs 6/100 (6.0)	56/552 (10.1) vs 63/553 (11.4)	0	0.89 (0.64—1.25)
Admission to the neonatal intensive	·	Not reported 40/292 (13.6) vs	19/160 (11.9) 8/160 (5.0) vs	6/100 (6.0) 8/100 (8.0) vs	19/260 (7.3) vs 25/260 (9.6) 56/552 (10.1) vs		

VA, not applicable

fewer instrumental vaginal deliveries than placebo and more cases of postpartum hemorrhage.²¹ Thomas et al²² showed that there are insufficient data to draw any conclusions regarding the efficacy of the combination of amniotomy with estrogen compared with estrogen alone as induction agents. Smyth et al⁴ performed a Cochrane review to determine the effectiveness and safety of amniotomy alone, compared with no amniotomy, for routinely shortening all labors that start spontaneously. They concluded that amniotomy alone vs intention to preserve the membranes resulted in similar length of labor and similar rate of cesarean delivery. Finally, Wei et al²³ aimed to estimate the effects of early augmentation with amniotomy and oxytocin for the prevention of or therapy for a delay in labor progress on the cesarean delivery birth rate and on indicators of maternal and neonatal morbidity. They concluded that, in prevention trials, early intervention with amniotomy and oxytocin appears to be associated with a modest reduction in the rate of cesarean delivery over standard care.²³ None of these Cochrane metaanalyses focused on just amniotomy after cervical ripening in the induction of labor, which instead was the focus of our metaanalysis.

Conclusion

In summary, routine early amniotomy, soon after cervical ripening in women with singleton gestations and cephalic presentation at term, does not increase the risk of cesarean delivery and reduces the interval from induction to delivery.

REFERENCES

1. ACOG Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 107:

- Induction of labor. Obstet Gynecol 2009;114: 386-97.
- 2. Garcia-Simon R, Montañes A, Clemente J, et al. Economic implications of labor induction. Int J Gynaecol Obstet 2015;133:125-5.
- 3. Maslow AS, Sweeny AL. Elective induction of labor as a risk factor for cesarean delivery among low-risk women at term. Obstet Gynecol 2000;95:917-22.
- 4. Smyth RMD, Alldred SK, Markham C. Amniotomy for shortening spontaneous labour. Cochrane Database Syst Rev 2007;4: CD006167.
- 5. Higgins JPT, Green S, editors. Cochrane handbook for systematic reviews of interventions, version 5.1.0 (update March 2011). The Cochrane Collaboration, 2011. Available at: training.cochrane.org/handbook. Accessed February 20, 2018.
- 6. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009;62:1006-12.
- 7. Levy R, Ferber A, Ben-Arie A, et al. A randomised comparison of early versus late amniotomy following cervical ripening with a Foley catheter. BJOG 2002;109:168-72.
- 8. Macones GA, Cahill A, Stamilio DM, Odibo AO. The efficacy of early amniotomy in nulliparous labor induction: a randomized controlled trial. Am J Obstet Gynecol 2012;207: 403.e1-5.
- 9. Makarem MH, Zahran KM, Abdellah MS, Karen MA. Early amniotomy after vaginal misoprostol for induction of labor: a randomized clinical trial. Arch Gynecol Obstet 2013;288:
- 10. Bostanci E, Eser A, Yayla Abide C, Kılıccı C, Kucukbas M. Early amniotomy after dinoprostone insert used for the induction of labor: a randomized clinical trial. J Matern Fetal Neonatal Med 2017:10:1-5.
- 11. Saccone G. Della Corte L. Maruotti GM. et al. Induction of labor at full-term in pregnant women with uncomplicated singleton pregnancy: a systematic review and meta-analysis of randomized trials. Acta Obstet Gynecol Scand 2019;98:958-66.
- ER. Saccone **12.** Magro-Malosso Chen M, Navathe R, Di Tommaso M, Berghella V. Induction of labour for suspected macrosomia at term in non-diabetic women: a systematic review and meta-

- analysis of randomized controlled trials. BJOG 2017;124:414-21.
- 13. Saccone G, Berghella V. Induction of labor at full term in uncomplicated singleton gestations: a systematic review and metaanalysis of randomized controlled trials. Am J Obstet Gvnecol 2015:213:629-36.
- 14. Magoga G, Saccone G, Al-Kouatly HB, et al. Warm perineal compresses during the second stage of labor for reducing perineal trauma: a meta-analysis. Eur J Obstet Gynecol Reprod Biol 2019;240:93-8.
- 15. Ehsanipoor RM, Saccone G, Seligman NS, Pierce-Williams RAM. Ciardulli A. Berghella V. Intravenous fluid rate for reduction of cesarean delivery rate in nulliparous women: a systematic review and meta-analysis. Acta Obstet Gynecol Scand 2017;96:804-11.
- 16. Saccone G, Ciardulli A, Baxter JK, et al. Discontinuing oxytocin infusion in the active phase of labor: a systematic review and metaanalysis. Obstet Gynecol 2017;130:1090-6.
- 17. Schoen CN, Saccone G, Backley S, et al. Increased single-balloon Foley catheter volume for induction of labor and time to delivery: a systematic review and meta-analysis. Acta Obstet Gynecol Scand 2018;97: 1051-60.
- 18. Ciardulli A, Saccone G, Anastasio H, Berghella V. Less-restrictive food intake during labor in low-risk singleton pregnancies: a systematic review and meta-analysis. Obstet Gynecol 2017;129:473-80.
- 19. Riegel M, Quist-Nelson J, Saccone G, et al. Dextrose intravenous fluid therapy in labor reduces the length of the first stage of labor. Eur J Obstet Gynecol Reprod Biol 2018;228:284-94.
- 20. Bricker L, Luckas M. Amniotomy alone for induction of labour. Cochrane Database Syst Rev 2000;4:CD002862.
- 21. Howarth GR, Botha DJ. Amniotomy plus intravenous oxytocin for induction of labour. Cochrane Database Svst Rev 2001:3: CD003250.
- 22. Thomas J, Kelly AJ, Kavanagh J. Oestrogens alone or with amniotomy for cervical ripening or induction of labour. Cochrane Database Syst Rev 2001;4:CD003393.
- 23. Wei S, Wo BL, Qi HP, et al. Early amniotomy and early oxytocin for prevention of, or therapy for, delay in first stage spontaneous labour compared with routine care. Cochrane Database Syst Rev 2013;8:CD006794.