Trial of labor after cesarean delivery in twin gestations: systematic review and meta-analysis

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BACKGROUND: Trial of labor after cesarean is offered as a routine option for singleton gestations with previous cesarean delivery. However, adequate data are not available to determine whether the approach is equally valid in women with twin gestation.

OBJECTIVE: This systematic review and meta-analysis aimed to assess maternal morbidities associated with trial of labor after cesarean delivery in twin gestations.

STUDY DESIGN: Electronic databases were searched for cohort studies and randomized controlled trials evaluating the association between trial of labor after cesarean delivery in twin gestations and pregnancy outcomes. Maternal mortality and severe morbidities, such as uterine rupture and hysterectomy, were compared between women who had trial of labor and women who had a planned repeat cesarean delivery. Pooled odds ratios were calculated using a random-effects model. Additional analyses were performed to compare trial of labor after cesarean outcomes in singleton and twin gestations.

RESULTS: Eleven cohort studies including a total of 8209 twin gestations with previous cesarean delivery were included in the present study. Of these gestations, 2484 were intended for planned vaginal birth and 5725 were intended for planned repeat cesarean delivery. The rate of uterine rupture in twin gestations was higher in the trial of labor after cesarean group than the elective cesarean group (odds ratio, 10.09, 95% confidence interval, 4.30–23.69, $I^2 = 68\%$). However, no statistically significant difference was found in the rate of uterine rupture between twin and single gestations attempting trial of labor after cesarean delivery (odds ratio, 1.34, 95% confidence interval, 0.54–3.31, $I^2 = 0\%$). Women who attempted a trial of labor after cesarean delivery with twins did not have an increased risk of uterine scar dehiscence, hemorrhage, blood transfusion, or neonatal morbidity and mortality compared with elective repeat cesarean delivery. Patients with twins had similar rates of successful vaginal delivery as patients with singletons (odds ratio, 0.85, 95% confidence interval, 0.61–1.18, $I^2 = 36\%$).

CONCLUSION: This meta-analysis demonstrates that, although trial of labor with twins after previous cesarean delivery is associated with higher rates of uterine rupture compared with elective cesarean delivery, pregnancy outcomes and success rates are similar to a trial of labor after previous cesarean delivery in singleton gestations. Planned vaginal birth for women with twin gestation and previous cesarean delivery may be a safe alternative to a planned repeat cesarean.

Keywords: cesarean delivery, trial of labor, elective vaginal birth after cesarean

Twin gestation rates have increased dramatically over the last 3 decades because of assisted reproductive technology and older maternal age at childbirth.[1–3] Multiple gestation pregnancies carry significant maternal and perinatal risks, making it one of the most common high-risk conditions in pregnancy encountered by obstetricians,[4–16] and a lack of consensus exists on the optimal mode of delivery.[17–30] Using the Robson Ten Group Classification System, Hehir et al[31] reported that the cesarean delivery rates for multiple pregnancies have steadily increased to >70% in recent years, which is similar to previous studies.[32,33]

The evolution in the mode of delivery management after cesarean is fascinating and can be tracked through several key publications over the past 30 years. In 1988, as a result of the increasing rate of cesarean delivery in the United States and several reports describing safe experiences with trial of labor after cesarean,[34] the American College of Obstetricians and Gynecologists (ACOG) published "Guidelines for Vaginal Delivery after a Previous Cesarean Birth," endorsing trial of labor as a safe and effective procedure to reduce cesarean delivery rates.[35]

Following these recommendations, the rate of trial of labor after cesarean delivery increased dramatically, exceeding 60% in many countries.[36] Subsequently, because of the publication of several reports suggesting an association between trial of labor and uterine rupture,[37,38] the ACOG issued another document in 1999 that recognized the possible adverse outcomes related to trial of labor after cesarean delivery.[39] The documents reflect changes in the approach and suggest offering trial of labor instead of encouraging it.

After this publication, trial of labor rates decreased remarkably as patients and physicians had become more risk averse and preferred to choose a safe

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AJOG at a Glance

Why was this study conducted?

We assessed adverse maternal and neonatal outcomes and compared them with repeated elective cesarean delivery in twin gestation and with trial of labor in singleton gestation.

Key findings

The key findings include the following: (1) the rate of uterine rupture in twin gestations was higher in the trial of labor group compared with the elective cesarean group; (2) uterine rupture rate did not differ between twin and singleton gestations attempting trial of labor after cesarean; and (3) trial of labor in twin gestations had similar risks and a similar likelihood of success as singleton pregnancies and could be an alternative to elective repeat cesarean section.

What does this add to what is known?

This meta-analysis shows that a trial of labor after cesarean delivery for women with twin gestation has similar risks and a similar likelihood of success as singleton pregnancies. Therefore, women with previous cesarean delivery who are otherwise appropriate candidates for twin vaginal delivery could be considered candidates for a trial of labor.

planned repeated cesarean delivery over a hazardous trial of labor. Since then, cesarean delivery rates for women with twin and singleton gestations and prior cesarean delivery have increased steadily in most developed countries.[40] There is growing concern regarding severe morbidities related to repeated cesarean delivery, resulting at least in part from the increase in elective repeat cesarean section over trial of labor.[27,41]

Women with a twin pregnancy and previous cesarean delivery are entitled to choose between planned elective repeat cesarean delivery or planned vaginal delivery.[42–44] There are benefits and harms associated with both options; therefore, making an informed decision may be challenging for both the women and their counseling physicians.[45,46]

The primary objective of a trial of labor is to increase the probability of having a successful vaginal delivery and to reduce cesarean delivery rates with subsequent reductions in cesarean delivery complications.[42,47] A Cochrane meta-analysis did not find significant differences between a planned cesarean birth and a planned vaginal birth for the primary outcomes of maternal death, severe morbidity, infant death, or severe infant morbidity in singleton gestation.[48]

A meta-analysis by Rossi et al[49] affirmed that pregnancy outcomes of trial of labor after cesarean delivery in singleton gestations are more favorable than those of elective repeat cesarean delivery. The meta-analysis demonstrated that a higher risk of uterine rupture in women planning a trial of labor is countered by a reduction in maternal morbidity, uterine dehiscence, and hysterectomy.

According to these findings and in the absence of contraindications, a trial of labor should be offered to every woman presenting with a singleton fetus at term.[44] Although it is now clear that a trial of labor after cesarean delivery is a reasonable and safe option for the majority of women with a singleton gestation, there are no adequate data to determine whether the approach is equally valid in women with a twin gestation and a previous cesarean delivery.[50]

The decision-making process between trial of labor and elective repeat cesarean delivery in twin gestation currently relies on limited data derived from cohort studies. A meta-analysis may provide more robust and reliable evidence regarding the benefits and harms of the delivery mode in women with twin gestation and previous cesarean birth.

The goals of this meta-analysis were to assess maternal and neonatal morbidity associated with a trial of labor after cesarean delivery in twin gestation compared with elective repeat cesarean delivery and the safety profile of a trial of labor in twin vs singleton gestations. Understanding the reasons and risk factors for increased morbidity in twin gestation with a previous cesarean delivery will allow physicians to perform appropriate patient counseling and improve the quality of patient care.

Materials and Methods

Data sources

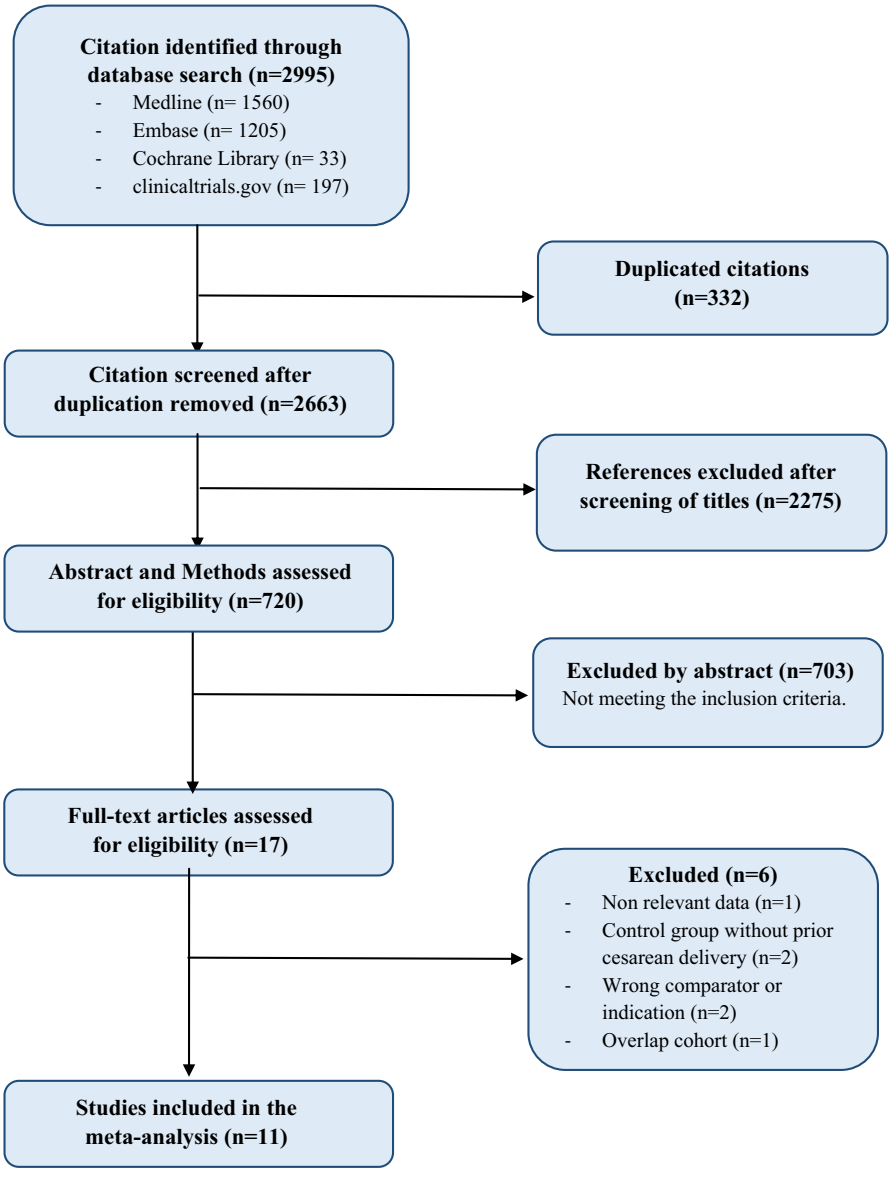
This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (2009) framework guidelines and the Meta-analysis Of Observational Studies in Epidemiology guidelines.[51,52] We conducted systematic manual searches in PubMed (MEDLINE), EMBASE, the Cochrane Library, and the Clinical Trials Registry (clinicaltrials.gov) to identify all randomized clinical trials, prospective observational studies, and retrospective cohort studies comparing trial of labor after cesarean delivery and elective repeat cesarean delivery in twin gestations published between 1996 and February 2017.

Relevant studies were identified using the following search terms: vaginal birth after cesarean, vaginal birth after cesarean, trial of labor, trial of labor, elective cesarean, elective cesarean, cesarean section, and repeat cesarean section. No language or date restrictions were applied. The detailed protocol is documented online in the International Prospective Register of Systematic Reviews registry (CRD42017080132). Because this study was a review and meta-analysis, no internal review board approval was required.

Selection criteria

The following screening criteria were applied to determine eligibility: cohort and cross-sectional studies of women in twin gestation comparing trial of labor after cesarean and elective repeat cesarean delivery. All cohort studies that reported safety data according to gestation were included. We excluded trials of T-shaped incisions or extensive transfundal uterine surgery, previous uterine rupture, or medical or obstetric complications that preclude vaginal delivery. Reviews and case reports were also excluded.

FIGURE 1
Publication selection and search process



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Study selection and data extraction

Two investigators (R.M. and N.S.-S.) independently identified and extracted articles for potential inclusion. Disagreements were resolved by referral to a third reviewer (D.K.). The full texts of the resulting references were then retrieved and analyzed. If more than a single study published data from the same cohort, we included the report with the higher quality according to Newcastle-Ottawa Quality Assessment Scale to avoid overlap.

The trial of labor in women with a previous cesarean delivery was defined in accordance with the criteria used by the included trials based on the following: previous low transverse cesarean delivery and no contraindication to vaginal birth. The primary endpoint of the present analysis was defined as uterine rupture, mortality or severe morbidity (eg, hysterectomy).

Quality assessment and risk of bias

Risk of bias and quality were assessed using the Newcastle-Ottawa Quality Assessment Scale (NOS) for assessing the quality of nonrandomized studies.[53] The scale is based on 8 criteria and provides a score ranging from 0 (high risk of bias) to 9 stars (low risk of bias). Summary assessments of the risk of bias were derived for each study. A 5 star rating and below was designated high risk of bias, 6−7 stars intermediate risk of bias, and 8−9 stars low risk of bias. Assessments were carried out independently by 2 investigators (R.M. and N.S.-S.).

Data synthesis and analysis

Analyses were performed using RevMan version 5.3 (The Nordic Cochrane Centre, the Cochrane Collaboration). Mantel-Haenszel random-effect pooled odds ratios (ORs) were calculated with the corresponding 95% confidence intervals (CIs) to summarize the results overall and within subgroups for trial of labor vs elective repeat cesarean delivery. In cases of zero events in both arms and because of the rarity of outcomes (eg, urine rupture), we used the Peto fixed odds ratio method to enable to pool results from all available studies with rare events, despite the high heterogeneity.

Publication bias

Publication bias was assessed by visual inspection of the funnel plot using RevMan 5.3. In the funnel plot, studies with a large number of participants appear toward the top of the graph and generally cluster around the mean effect size and a smaller SE. Studies with a small number of participants appear toward the bottom of the graph and tend to be spread across a broad range of effects size values and SEs.

Results

A total of 2994 citations were identified, 17 of which were retrieved for full-text review. Two studies reported data from the same cohort,[54,55] and the higher-quality study according to the NOS scale was included in our analysis.[55] Five more publications were excluded, leaving 11 studies for the final analysis. The studies were published between 1989 and 2010 and originated from the United States (n = 7), Asia (n = 2), Canada (n = 1), and Africa (n = 1). The selection process is illustrated in Figure 1.

TABLE 1
Main characteristics of the retrospective studies included in the meta-analysis

Study/year (country)	Study period	Intervention vs control group	Number of women TOLAC/sample	Primary and secondary outcome measures	Adjustment	Newcastle-Ottawa Score
Strong et al,[72] 1989 (United States)	1982–1986	Twin gestation: TOLAC vs ERCS	TOLAC, 25 ERCS, 31	Uterine dehiscence Hemorrhage Hysterectomy Perinatal mortality Apgar score	None	7
Miller et al,[56] 1996 (United States)	1985– 1994	Twin gestation: TOLAC vs ERCS	TOLAC, 92 ERCS, 118	Uterine rupture Maternal death Uterine dehiscence Blood transfusion Hysterectomy Perinatal mortality Apgar score	Gestational age	8
Odeh et al,[73] 1997 (Israel)	1970–1993	Twin gestation: TOLAC vs ERCS	TOLAC, 21 ERCS, 15	Uterine dehiscence Blood transfusion Apgar score	None	7
Aboulfalah et al,[62] 1999 (Morocco)	1994–1998	Twin gestation: TOLAC vs ERCS	TOLAC, 25 ERCS, 6	Perinatal mortality Apgar score	None	6
		TOLAC: twin vs singleton gestations	Twins, 25 Singleton, 250	Uterine rupture Successful TOLAC		
Myles,[41] 2001 (United States)	1991–1999	TOLAC: twin vs singleton gestations	Twins, 19 Singleton, 57	Uterine rupture Successful TOLAC	None	6
Sansregret et al,[60] 2002 (Canada)	1988–2001	Twin gestation: TOLAC vs ERCS	TOLAC, 26 ERCS, 71	Uterine rupture Hemorrhage Blood transfusion Hysterectomy Apgar score	None	7
Delaney and Young,[61] 2002 (United States)	1980–1999	Twin gestation: TOLAC vs ERCS	TOLAC, 38 ERCS, 83	Hemorrhage Perinatal mortality	Previous postpartum hemorrhage, thrombocytopenia, and acquired coagulation disorders	7
Varner et al,[57] 2005 (United States)	1999–2002	Twin gestation: TOLAC vs ERCS	TOLAC, 186 ERCS, 226	Uterine rupture Blood transfusion Perinatal mortality Apgar score	Gestational age	8
		TOLAC: twin vs singleton gestations	Twins, 186 Singleton, 17,897	Uterine rupture Successful TOLAC		

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(continued)

TABLE 1
Main characteristics of the retrospective studies included in the meta-analysis *(continued)*

Study/year (country)	Study period	Intervention vs control group	Number of women TOLAC/sample	Primary and secondary outcome measures	Adjustment	Newcastle-Ottawa Score
Cahill et al,[58] 2005 (United States)	1996–2000	TOLAC: twin vs singleton gestations	Twins, 177 Singleton, 13,427	Uterine rupture Successful TOLAC	Previous vaginal deliveries and hysterotomies, maternal age, gestational age, macrosomia, diabetes mellitus, hospital type, and labor methods (spontaneous, induced, or augmented)	8
Ford et al,[59] 2006 (United States)	1993–2002	Twin gestation: TOLAC vs ERCS	TOLAC, 1850 ERCS, 4705	Uterine rupture Uterine dehiscence Blood transfusion Hysterectomy	None	7
Aaronson et al,[55] 2010 (Israel)	1988–2007	Twin gestation: TOLAC vs ERCS	TOLAC, 25 ERCS, 109	Uterine rupture Maternal mortality Blood transfusion Perinatal mortality Apgar score	Gestational age, maternal age, ethnicity, and fetal malformations	9

ERCS, elective repeat cesarean section; *TOLAC*, trial of labor after cesarean.
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The 11 studies included 8209 women with twin gestations and a previous cesarean delivery; 5725 underwent planned elective repeat cesarean delivery and 2484 attempted vaginal delivery. Seven of the studies exclusively compared trial of labor after cesarean and elective repeat cesarean section, 2 studies included a comparison between a twin and singleton trial of labor after cesarean delivery, and 2 studies included both comparisons. Table 1 provides the major characteristics of the studies.

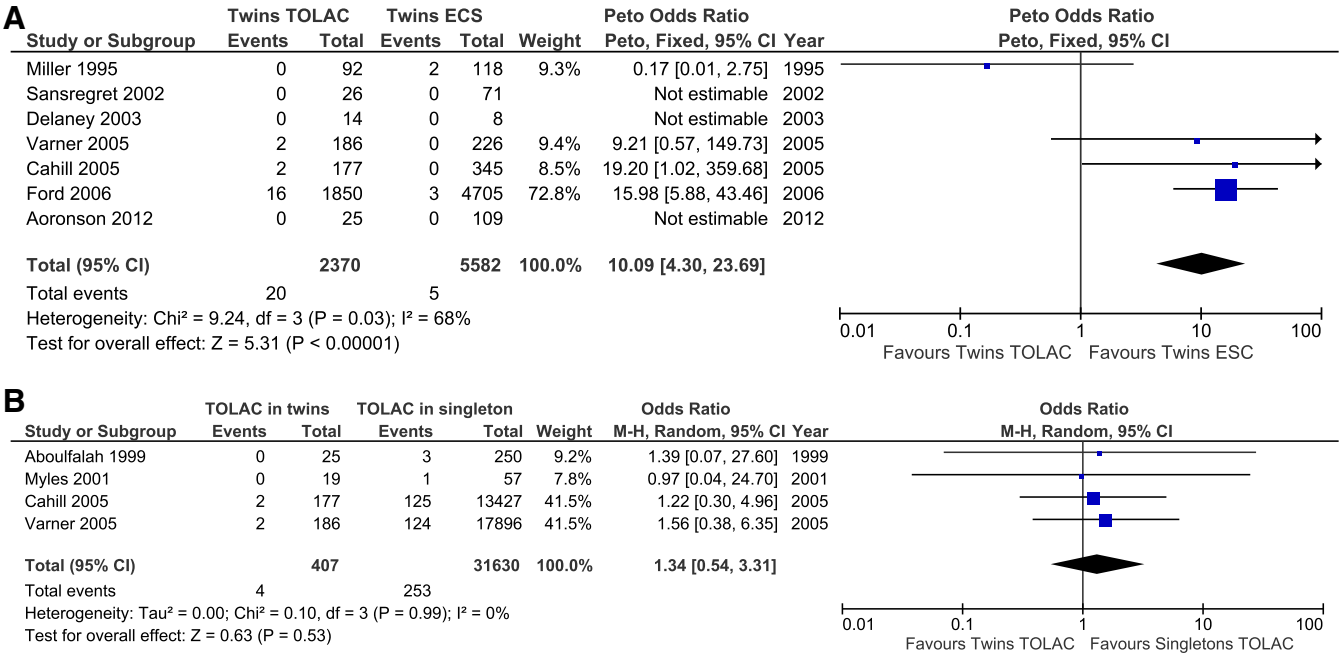
Seven studies have compared uterine rupture rates after trial of labor vs elective repeat cesarean delivery in twin gestations; 2 reported no significant difference between the groups,[56,57] 2 reported an increased uterine rupture rate after trial of labor,[58,59] and the other 3 studies reported zero events in both arms[55,60,61] (Figure 2A). When evaluating uterine rupture rates between singletons and twins after successful vaginal delivery, 4 studies have reported no difference (Figure 2B).[41,57,58,62]

Trial of labor after cesarean delivery in women with a twin gestation was associated with a higher rate of uterine rupture compared with elective repeat cesarean delivery (OR, 10.09, 95% CI, 4.30–23.69, I^2 = 68%; Figure 2A). However, no statistically significant difference was found in the uterine rupture rates between twin and singleton gestations attempting a trial of labor (OR, 1.34, 95% CI 0.54–3.31, I^2 = 0%; Figure 2B).

Four studies provided data that allowed us to compare the success rate for singleton and twin gestations opting for vaginal delivery after cesarean.[41,57,58,62] Women with twin gestations had similar rates of successful vaginal delivery as women with singleton gestations (OR, 0.85, 95% CI, 0.61–1.18, I^2 = 36%; Figure 3).

Women who attempted a trial of labor with twins had no increased risk of uterine scar dehiscence (OR, 1.52, 95% CI, 0.72–3.19, I^2 = 0%; Figure 4A), hemorrhage (OR, 0.95, 95% CI, 0.19–4.76, I^2 = 83%; Figure 4B), blood transfusion (OR, 0.82, 95% CI, 0.56–1.20, I^2 = 0%; Figure 4C), or hysterectomy (OR, 0.50, 95% CI,

FIGURE 2
Uterine rupture in VBAC and TOLAC



A, Uterine rupture in twin gestations planning vs those opting for an ERC. Forest plot of the odds ratio for uterine rupture in the cohort studies is shown. The forest plot presents odd ratios for uterine rupture in twin gestations following a trial of labor after cesarean section vs elective repeat cesarean delivery. **B,** Uterine rupture in women attempting a trial of labor after cesarean delivery in twin vs singleton gestations. Forest plot of the odds ratio for uterine rupture in cohort studies is shown. The forest plot presents odd ratios for uterine rupture in trial of labor after cesarean section of twin gestation vs singleton gestation.

ECS, elective cesarean section; *TOLAC*, trial of labor after cesarean; *VBAC*, vaginal birth after cesarean.

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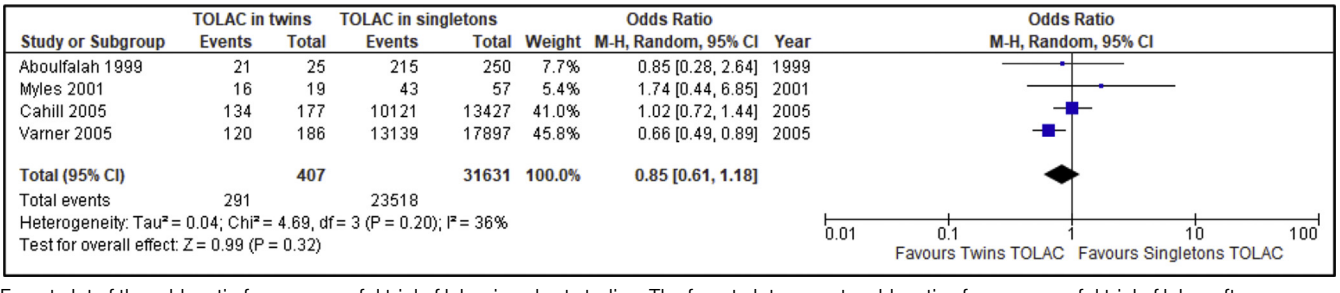
0.24–1.08, I^2 = 0%; Figure 4D) compared with elective repeat cesarean delivery.

We were unable to assess maternal mortality as an outcome in this meta-analysis because only 2 of our selected publications reported this outcome. Miller et al[56] reported no cases of maternal mortality, whereas a single case of maternal mortality in women with planned elective cesarean delivery was reported by Aaronson et al.[55]

Maternal mortality appeared to be very low in both studies. Similarly, no

FIGURE 3
A successful TOLAC in twin vs singleton gestations



Forest plot of the odds ratio for a successful trial of labor in cohort studies. The forest plot presents odds ratios for a successful trial of labor after cesarean section of twin gestation vs a singleton gestation.

TOLAC, trial of labor after cesarean.

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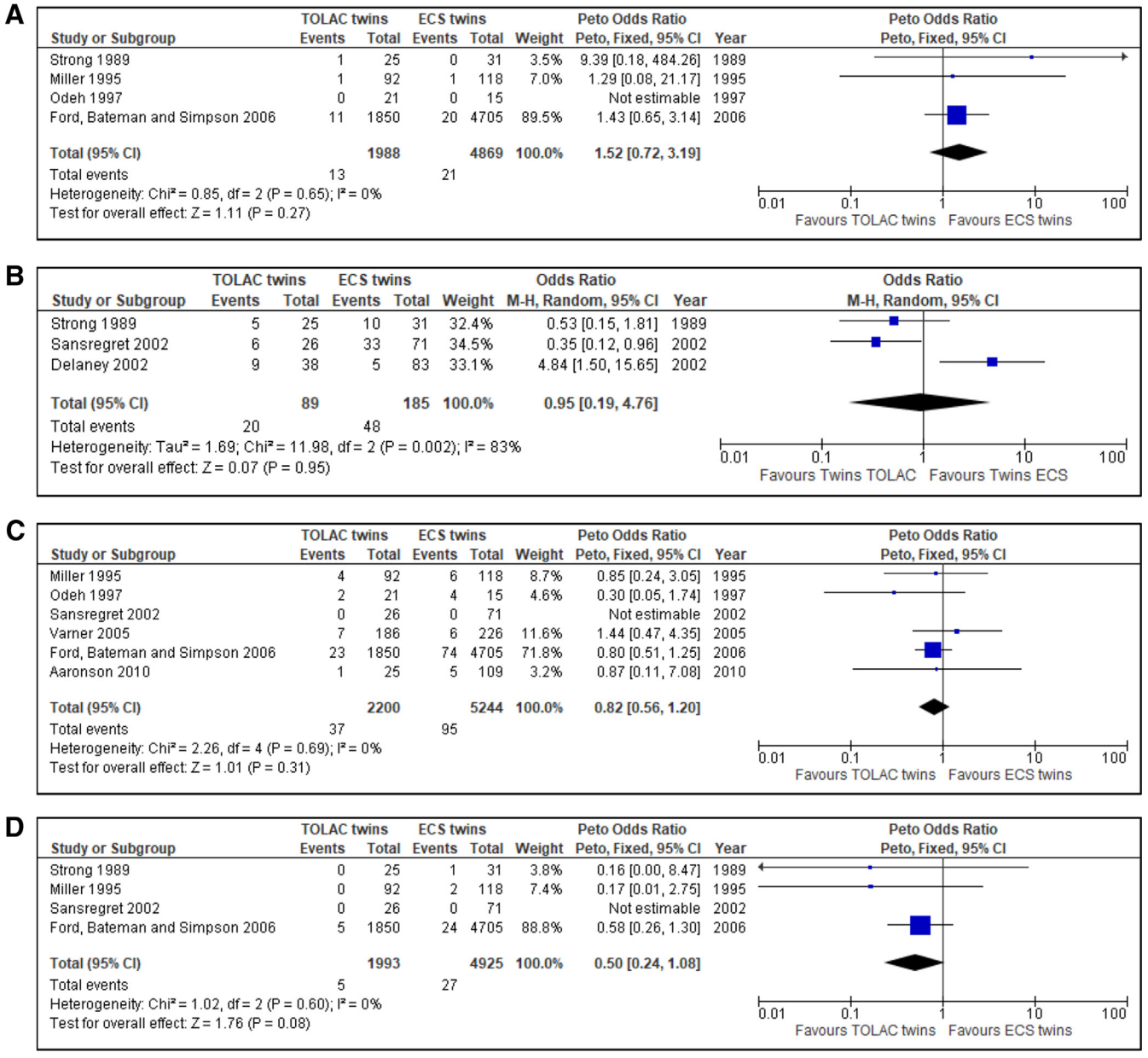
FIGURE 4
Forest plots of OR for maternal outcomes in cohort studies



A, The forest plot presents odd ratios for uterine scar dehiscence in twin gestations following a trial of labor after cesarean section vs elective repeat cesarean delivery. **B,** The forest plot presents odd ratios for hemorrhage in twin gestations following a trial of labor after cesarean section vs elective repeat cesarean delivery. **C,** The forest plot presents odd ratios for blood transfusion in twin gestations following a trial of labor after cesarean section vs elective repeat cesarean delivery. **D,** The forest plot presents odd ratios for hysterectomy in twin gestations following a trial of labor after cesarean delivery vs elective repeat cesarean delivery.

OR, odds ratio.

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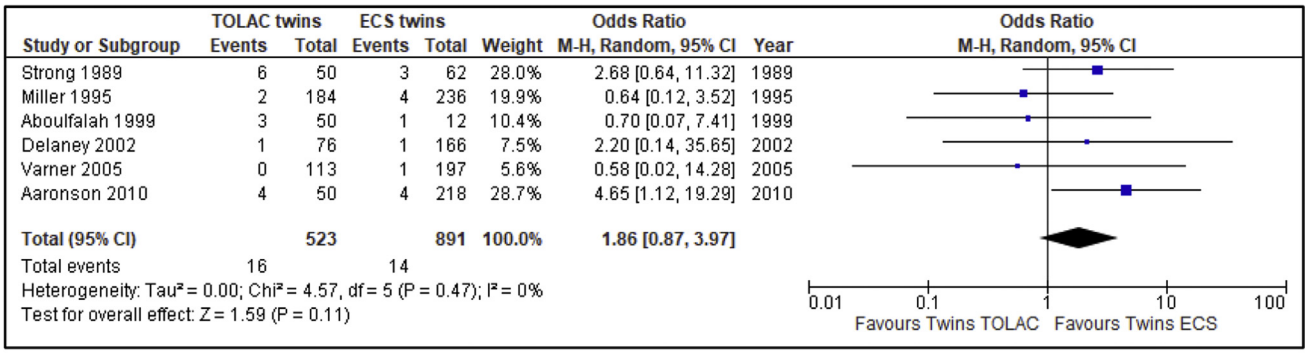
significant differences were found following a trial of labor after cesarean vs elective repeat cesarean delivery for twin gestations in perinatal mortality (OR, 1.86, 95% CI, 0.87−3.97, I^2 = 0%; Figure 5A) and Apgar score <7 at 5 minutes (OR, 0.86, 95% CI, 0.46−1.60, I^2 = 0%; Figure 5B).

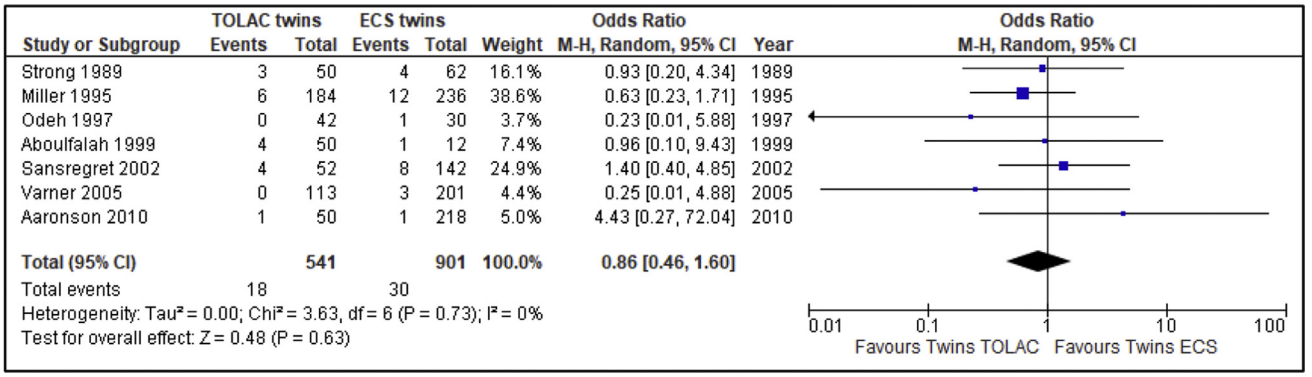
A quality assessment of the nonrandomized studies was performed using the NOS (Table 2). Four studies scored 8 and 9 (low risk of bias), whereas

FIGURE 5
Forest plots of OR for neonatal outcomes in cohort studies

A



B



A, The forest plot presents odd ratios for perinatal mortality in twin gestations following a trial of labor after cesarean delivery vs elective repeat cesarean delivery. **B,** The forest plot presents odd ratios for Apgar score <7 at 5 minutes after delivery in twin gestations following a trial of labor after cesarean delivery vs elective repeat cesarean delivery.

OR, odds ratio.

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7 studies scored 7 and 6 (intermediate risk of bias). After examining the funnel plots for publication bias, subjective impressions support the presence of a symmetrical inverted funnel, indicating that the probability of publication bias is very low. Although the distribution of studies appears to be symmetrical, the small number of studies cannot exclude the possibility of publication bias. Funnel plots are not presented because of a small number of studies for the outcome measured.

Comment

Our study shows that, although the rate of uterine rupture in twin gestations was higher in the trial of labor after cesarean group compared with the elective repeat cesarean delivery group, it did not differ between twin and single gestations attempting a trial of labor. Moreover, a trial of labor in twin gestations had similar risks and a similar likelihood of success as singleton pregnancies and could be an alternative to elective repeat cesarean delivery. This information should be provided during antenatal counseling and individualized to women's circumstances and plans for future fertility.

The principal risk associated with trial of labor after cesarean delivery is a uterine rupture. Many studies have demonstrated that uterine rupture rates are higher in women with a trial of labor than in women opting for elective repeat cesarean delivery.[49,63–68] This outcome is not surprising because the majority of women with planned elective cesarean deliveries do not experience uterine contraction, which is considered the major event for uterine rupture.

In these cases, the uterine scar remains unchallenged and the likelihood of uterine rupture decreases significantly. Although uterine rupture rates are higher in twin gestation attempting a trial of labor after cesarean delivery, it is considered a safe and acceptable delivery option because the absolute risk of adverse outcomes is extremely low.

The mechanisms responsible for uterine rupture in women with previous cesarean delivery are unknown.[69] Uterine overdistention associated with multifetal pregnancy may generate mechanical changes affecting the uterine scar, decreasing its stability against uterine contractions.[62,69,70] Few studies addressed this question and failed to demonstrate any association between uterine overdistention and increased occurrence of uterine rupture.[36,58–61,71–75] Fisk et al[76] showed that the intraamniotic pressure

TABLE 2
Risk of bias in each included study: a quality assessment using the Newcastle-Ottawa Scale[53]

	Selection				Comparability	Outcomes		
Representativeness of the exposed cohort	Representativeness of the exposed cohort	Selection of the nonexposed cohort	Ascertainment of exposure	Demonstration that the outcome of interest was not present at the start of the study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts
Strong et al,[72] 1989	B	A	A	A	?	B	A	A
Miller et al,[56] 1995	B	A	A	A	A	B	A	A
Odeh et al,[73] 1997	B	A	A	A	?	B	A	A
Aboulfalah et al,[62] 1999	B	A	A	B	?	B	A	A
Myles,[41] 2001	B	B	A	A	?	B	A	A
Sansregret et al,[60] 2002	B	A	A	A	?	B	A	A
Delaney and Young,[61] 2002	B	A	A	A	?	B	A	A
Varner et al,[57] 2005	B	A	A	A	A	B	A	A
Cahill et al,[58] 2005	A	B	A	A	A B	B	A	A
Ford et al,[59] 2006	A	A	A	A	?	B	A	A
Aaronson et al,[55] 2010	B	A	A	A	A B	B	A	A

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does not differ between twin and singleton gestations. Furthermore, in contrast to several previous studies,[56,61,72] we did not find any association between a trial of labor after cesarean delivery for twin gestation and increased neonatal death.

An evaluation of the safety profile of a trial of labor after cesarean delivery for twin gestation should include a comparison with a singleton gestation. Previous studies have reported similar outcomes and successful vaginal birth rates after cesarean delivery for twin pregnancies as in singleton pregnancies.

In this meta-analysis, we did not find differences in uterine rupture rates and adverse maternal and neonatal outcomes between women with twin vs singleton gestations opting for a trial of labor after cesarean delivery. The uterine rupture rate was less than 1% while the success rate was greater than 70% in both groups. Therefore, our results confirm that the safety profile of a trial of labor after cesarean delivery is similar between twin and singleton gestation and can be considered satisfactory.

The latest guidelines of ACOG, the Royal College of Obstetricians and Gynaecologists, and other organizations of women's health care physicians worldwide affirmed that twin gestation is not a contraindication to a trial of labor after cesarean delivery.[42–44,50,77,78] The results of this meta-analysis support this conclusion and increase the quality of the evidence.

Strengths and limitations

This is the largest study to pool results for maternal morbidity among women with twin gestations and previous cesarean delivery. This meta-analysis included all available published data, conducted systematically and according to accepted guidelines. Because the studies included in this meta-analysis are retrospective, selection bias should be considered and evaluated. We performed a quality assessment for bias risk using the NOS, which resulted in a low probability of selection bias. Because of the small number of studies and events, our results need to be interpreted with

caution, and further studies are required to confirm our results.

The cohorts included in this meta-analysis were geographically and racially diverse, which can potentially be considered as both a strength and limitation of this analysis. Different countries represent women from different ethnic groups, broadening the generalizability of our results. The potential weakness rests with the increased heterogeneity of management and the lack of standardization.

Some of our analyses had high heterogeneity, and we used random-effect models, when not pooling rare events, to reduce the effects of heterogeneity on the assessed outcomes. The inclusion of zero events in both treatment arms is controversial. It is thought that these events do not make a significant contribution to the measured outcome. However, zero events provide critical information regarding the available data and the rarity of the measure's outcome. Therefore, in cases of zero events of both arms, we used the Peto fixed method to pool results to assess the true effect size.

We did not use the continuity correction method for meta-analysis of rare adverse events because it may introduce bias into the analysis. The exclusion of zero events in both arms may increase the effect size and including them may decrease the effects size.[79] Therefore, our results of analyses with zero events in both arms needed to be interpreted carefully.

In this meta-analysis, we pooled together heterogeneous studies in which several studies by Delaney and Young,[61] Cahill et al,[58] and Aaronson et al[55] adjusted their analysis to several confounders, including gestational age and delivery methods, and other studies did not perform adjustment to confounders. Therefore, there is always the possibility that our results may not reflect the true effect size and may be susceptible to different sources of bias. Although the studies are heterogeneous, they represent real-life conditions, and therefore, we decided to pool the results together to examine the direction of the outcomes.

In conclusion, this meta-analysis shows that a trial of labor after cesarean delivery for women with twin gestations has similar risks and a similar likelihood of success as singleton pregnancies. Therefore, women with a previous cesarean delivery who are otherwise appropriate candidates for twin vaginal delivery and have no other contraindications could be considered candidates for a trial of labor. Although the rate of uterine rupture in twin gestation was higher in the trial of labor group compared with the elective repeat cesarean delivery group, it may still be considered a safe and acceptable delivery option because the absolute risk is extremely low. Furthermore, individualized assessment and a cautious approach are advised if planned vaginal delivery is being considered. ■

ACKNOWLEDGMENT

The trial registry in the International Prospective Register of Systematic Reviews registry has a number of CRD42017080132 (http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017080132).

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