OBSTETRICS

Maternal morbidity following a trial of labor after cesarean section vs elective repeat cesarean delivery: a systematic review with metaanalysis

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This study reviewed maternal morbidity following trial of labor (TOL) after cesarean section, compared with elective repeat cesarean delivery (ERCS). Articles were pooled to compare women planning vaginal birth after cesarean (VBAC) with those undergoing ERCS with regard to maternal morbidity (MM), uterine rupture/dehiscence (UR/D), blood transfusion (BT), and hysterectomy. The former group was subdivided into successful VBAC (S-VBAC) and failed TOL (F-TOL). VBAC was successful in 17,905 of 24,349 patients (73%). MM, BT, and hysterectomy were similar in women planning VBAC or ERCS, whereas UR/D was different (1.3%; 0.4%). MM, UR/D, BT and hysterectomy were more common after F-TOL (17%, 4.4%, 3%; 0.5%) than after S-VBAC (3.1%, 0.2%, 1.1%; 0.1%) or ERCS (4.3%, 0.4%, 1%; 0.3%). Outcomes were more favorable in S-VBAC than ERCS. These findings show that a higher risk of UR/D in women planning VBAC than ERCS is counterbalanced by reduction of MM, UR/D, and hysterectomy when VBAC is successful.

Key words: elective repeat cesarean delivery, trial of labor, uterine dehiscence, uterine rupture, vaginal birth after cesarean section

Before the 1970s, deliveries by cesarean section were considered as indication for cesarean section in the subsequent pregnancies, reflecting a concern that uterine scar tissue might rupture during labor. In the 1980s, the dictum “once a cesarean, always a cesarean,” espoused by Craighin in 1916, was revised in many countries, and a trial of labor in women with history of cesarean section was proposed as an attempt to reduce cesarean section rates. However, an apparent increase in the incidence of uterine rupture and concern about maternal and fetal safety have challenged the choice of vaginal delivery in women having a scarred uterus. As a consequence, clinicians are increasingly being faced in deciding the mode of delivery in pregnant women whose first delivery was by cesarean section.

A metaanalysis of articles published in the period 1982-1989 failed to identify advantages for elective repeat cesarean delivery, compared with trial of labor, with regard to uterine rupture and perinatal death. In contrast, a metaanalysis of subsequent investigations published from 1989 to 1999 reported a higher rate of uterine rupture and perinatal death following a trial of labor than following elective cesarean section. The aim of this study was to review publications available in literature from the period of 2000 through 2007, which compared maternal morbidity after a trial of labor vs elective repeat cesarean delivery and assessed risk factors for failure of vaginal birth after cesarean delivery.

Materials and methods

A search in PubMed was performed in the period 2000-2007 to find relevant articles that compared maternal morbidity in women who had a trial of labor (TOL) vs women undergoing elective repeat cesarean section (ERCS) without labor and/or analyzed risk factors for unsuccessful TOL. Key words were vaginal birth after cesarean section (VBAC), uterine rupture, uterine dehiscence, previous cesarean, caesarean section, risk factors, trial of labor, and uterine scar. Articles were included in review and metaanalysis if they met the following inclusion criteria: rate of TOL and ERCS clearly reported in tables or text, failed TOL (F-TOL) defined as the rate of patients who planned VBAC but subsequently delivered by emergency cesarean section and study population represented by singleton pregnancies with delivery after 20 weeks of gestation, or a newborn infant weighting 500 g or more. Exclusion criteria were omitting of at least 1 inclusion criterion; induction of labor for termination of pregnancy or intrauterine fetal death; studies performed in selected population, such as multiparous women, postterm pregnancies, and multiple pregnancies; studies conducted in developing countries because of differences in medical practice; and number of subjects in the TOL and ERCS groups reported in graphs or percentage. Letters, comments, reviews, personal communications, and non–English-language publications were also excluded.

The study population was divided into 2 groups: patients who planned VBAC and patients who planned ERCS. The first group was further subdivided into women who successfully delivered vaginally and women who failed a trial of labor and underwent emergency cesarean section (F-TOL). The following comparisons were performed with regard to any type of maternal morbidity, uterine rupture/dehiscence, and medical interven-
tigated the risk factors for failure of a TOL.

**Maternal morbidity analysis**

Maternal morbidity was compared between planned VBAC and planned ERCS in 7 studies. They were pooled for metaanalysis and provided 24,349 (57%) women who planned VBAC and 18,621 (43%) who planned ERCS. Women who attempted VBAC were further subdivided in a successful VBAC group and a F-TOL group for a total of 17,905 (73%) and 6444 (27%) women, respectively. Therefore, the overall successful rate of vaginal delivery in patients who attempted a trial of labor after previous cesarean section was 73% (range 68% to 77%).

The Table shows the characteristics of each study. The incidence of maternal morbidity, uterine rupture/dehiscence, blood transfusion, and hysterectomy in each study group is represented in Figure 1.

**Planning VBAC vs ERCS**

Three studies were concordant in finding a higher maternal morbidity rate when VBAC was planned in contrast to ERCS, whereas 4 studies did not report a significant difference between the 2 modes of delivery. Metaanalysis showed that maternal morbidity did not differ between women planning VBAC and patients undergoing ERCS (planned VBAC: 1642 of 24,349, 6.7%; ERCS: 757 of 18,621, 4%; Z = 1.55; P = .12). Uterine rupture/dehiscence was reported in each investigation and incidence ranged from 0% to 6.7% in the planned VBAC group and from 0% to 1.5% in ERCS group.

Three studies observed a higher incidence of uterine rupture/dehiscence in women planning VBAC, compared with women choosing ERCS. Metaanalysis showed a significant difference in uterine rupture/dehiscence between the 2 groups (planning VBAC: 320 of 24,349; 1.3%; ERCS: 80 of 18,621; 0.4%; Z = 2.55; P = .01; OR 3.13; 95% CI 1.30 to 7.50) (Figure 2).

Blood transfusion was reported in 5 studies. Overall, it was required in 362 of 20,928 (1.7%) cases of planned VBAC and 187 of 17,259 (1.2%) cases of ERCS without differences between the 2 groups (Z = 0.18; P = .86).

Hysterectomy was reported in 5 studies, of which in only 1 the procedure was not necessary in any group, and in the other 4 articles, no differences were noted between women planning VBAC and women undergoing ERCS. Considered as a whole, hysterectomy was performed in 52 of 23,448 (0.2%) cases of planned VBAC and 49 of 17,827 (0.3%) cases of ERCS without a significant difference (Z = 1.00; P = .32).

**Successful VBAC vs F-TOL**

Six studies compared maternal morbidity and uterine rupture/dehiscence in women with successful VBAC vs those for whom a TOL failed. All the studies were concordant in finding a lower morbidity rate in women destined to deliver vaginally, compared with women with F-TOL. Metaanalysis confirmed that maternal complications occurred less frequently in the successful VBAC (533 of 17,358; 3.1%) than the F-TOL group (1062 of 6223; 17%; Z = 6.66; P < .0001; OR 0.15; 95% CI, 0.09 to 0.26) (Figure 3, A). When VBAC was successful, uterine rupture/dehiscence occurred in 0% to 0.4%, whereas in women experiencing F-TOL, uterine rupture/dehiscence ranged from 0% to 6.7%. All but 1 study found a decreased risk of uterine rupture/dehiscence in women with successful VBAC, compared with women with F-TOL. Metaanalysis reported that women with successful VBAC were affected with uterine rupture/dehiscence less frequently than woman in the F-TOL group (successful VBAC: 39 of 17,358; 0.2% vs F-TOL: 279 of 6223; 4.4%; Z = 6.30; P < .0001; OR 0.05; 95% CI 0.02 to 0.13) (Figure 3, B).

Four studies assessed blood transfusion in successful VBAC and F-TOL. The pooled analysis showed that women with successful VBAC (162 of 14,766; 1.1%) required blood transfusion less frequently than women with F-TOL (164 of 5394; 3%; Z = 9.35; P < .0001; OR 0.35; 95% CI, 0.28 to 0.44) (Figure 3, C).

In 3 studies hysterectomy was stratified for successful VBAC and F-TOL
groups, and results were controversial: in 1 article, the surgical procedure was not performed in any groups, in another article, hysterectomy was equally necessary in both the 2 groups, and in a third article, women with successful VBAC were less likely to undergo hysterectomy than women with F-TOL. The meta-analysis of these 3 articles proved that successful VBAC (21 of 14,189; 0.1%) was less likely associated with hysterectomy than F-TOL (26 of 5217; 0.5%; Z = 4.09; P < .0001; OR 0.30; 95% CI, 0.17 to 0.53) (Figure 3, D).

**F-TOL vs ERCS**

Comparison of maternal morbidity and uterine rupture/dehiscence between F-TOL and ERCS was performed in 6 articles. All but 1 study were concordant in detecting a higher rate of maternal morbidity when TOL failed than when ERCS was performed. Considered as a whole, maternal complications occurred less frequently in the ERCS (738 of 18,389; 4.3%) group than the F-TOL group (1062 of 6223; 17%; Z = 6.64; P < .0001; OR 0.25; 95% CI, 0.16 to 0.37) (Figure 4, A). When the incidence of uterine rupture/dehiscence was stratified in the F-TOL and ERCS groups, 2 investigations reported a similar rate in the 2 groups, whereas the other 4 articles observed a lower rate of uterine rupture/dehiscence in favor of ERCS. Metaanalysis showed that uterine rupture/dehiscence was higher in the F-TOL group than ERCS (279 of 6223; 4.4% vs 80 of 18,389; 0.4%, respectively; Z = 4.28; P < .0001; OR 11.34; 95% CI, 3.73 to 34.50) (Figure 4, B).

Similarly, in 4 studies, the incidence of blood transfusion was higher in
F-TOL than ERCS (164 of 5393; 3% vs 170 of 17027; 1%; Z = 10.04; P < .0001; OR 3.05; 95% CI, 2.45 to 3.80) (Figure 4, C). No differences were detected in hysterectomy between F-TOL and ERCS in either single investigations or metaanalysis (F-TOL: 26 of 5217, 0.5% vs ERCS: 47 of 16,300; 0.3%; Z = 1.09; P = .27).

Successful VBAC vs ERCS
Maternal morbidity, distinguished between the 2 groups in 6 publications, was slightly lower following successful VBAC (533 of 177358; 3.1%) than ERCS (738 of 18389; 4%), although the statistical difference was minimal (Z = 2.11; P = .04; OR 0.74; 95% CI, 0.56 to 0.98) (Figure 5, A).

Similarly, uterine rupture/dehiscence occurred less frequently in women with successful VBAC (39 of 177358; 0.2%) than women undergoing ERCS (80 of 18389; 0.4%; Z = 3.14; P = .002; OR 0.54; 95% CI, 0.37 to 0.79) (Figure 5, B).

The pooled analysis of four studies also showed that 162 of 14,766 (1.1%) women with successful VBAC required blood transfusion as well as women with ERCS (170 of 17,027; 1%; Z = 0.72; P = .47). In three studies hysterectomy was stratified for the success of VBAC and ERCS groups, of which in 2 studies there was not a statistical difference, and 1 publication reported results in favor of successful VBAC women. The metaanalysis of these 3 articles proved that successful VBAC (21 of 14,189; 0.1%) was less likely related to hysterectomy than the overall risk of uterine rupture was significantly higher following labor induction, compared with spontaneous labor (induced labor: 208 of 15,018; 1.3%; spontaneous labor: 184 of 34,236; 0.5%; Z = 6.95; P < .0001; OR 2.83; 95% CI, 2.11 to 3.80) (Figure 6).

COMMENT
This review shows that TOL after previous cesarean section is associated with a successful rate of 73%, and the incidence of maternal morbidity is similar in women experiencing a TOL and women choosing ERCS. Uterine injury occurs in 1.3% and 0.4% of women undergoing TOL and ERCS, respectively, and the risk of uterine lesions is 3-fold greater in patients planning VBAC, compared with those undergoing ERCS. Additional interventions, in particular blood transfusion and hysterectomy, are performed with the same frequency in the 2 groups. Our findings are similar to the results presented in metaanalysis by Mozurkewich and Hutton, although the incidence of uterine lesions was lower than the incidence reported in our analysis. A possible explanation may be that in the previous review, only symptomatic ruptures were analyzed, whereas in our paper dehiscence was also considered for analysis.

We did further comparison between failed vs successful VBAC as well as vs ERCS. In this analysis we determined that women who experienced failure of VBAC present an increased risk of maternal adverse outcomes, compared with both latter groups. In particular, when a TOL fails, maternal morbidity is 17%, which is much higher than 3.1% assessed in women destined to successful vaginal delivery.

Risk factor analysis
Twelve articles assessed risk factors for failure of a TOL but could not be pooled in a metaanalysis because the study groups were not comparable. In these studies, factors that have been associated with F-TOL included the following: short interpregnancy interval,14 birthweight,15 no history of previous vaginal delivery,16-21 maternal diabetes,16 obesity,22,23 excessive weight gain,2 patients with multiple prior cesarean deliveries,24 cephalopelvic disproportion,21 alcohol and cigarette use, and lesser degrees of cervical dilatation at admission.20,25

The risk of uterine rupture/dehiscence after induction of labor in women with previous cesarean section and attempting VBAC in the next pregnancy could be assessed with metaanalysis. Nine publications were reviewed. Induction of labor was achieved with prostaglandins and/or oxytocin in 6 studies,8,10,11,26-28 only prostaglandins in 2 investigations,29,30 and only oxytocin in another publication.19 Seven studies were concordant in determining a higher incidence of uterine lesion following induced labor, compared with spontaneous onset of labor, whereas in 2 studies,27,28 no statistical difference was detected between the 2 groups. The metaanalysis calculated that the overall risk of uterine rupture was 2.11; P = .04; OR 0.74; 95% CI, 0.56 to 0.98 (Figure 5, A).

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delivery. Uterine lesions are also observed more often following a failed TOL (4.4%), in contrast to a successful VBAC (0.2%), and this finding might explain why blood transfusion and hysterectomy are more often required in the former than the latter group. These findings suggest that, when TOL fails, adverse outcomes are more likely to occur than when VBAC is successful.

The differences that we observed between women in which VBAC ended successfully and those who underwent ERCS are in contrast to our expectation but are probably not clinically meaningful and may depend on the small number of studies, of which 11 contributed with a very high weight in the metaanalysis.

Because the increased maternal morbidity in women attempting a TOL is primarily detected when TOL fails, the identification of factors associated with failed TOL is mandatory in selecting patients who may be considered as VBAC candidates. Therefore, many studies focused on risk or predictive factors of unsuccessful VBAC. History of a previous spontaneous vaginal delivery before the initial cesarean delivery has been revealed as a good predictor for successful TOL. Kayani and Alfirevic observed that of 107 women with previous cesarean section but no history of vaginal delivery, induction of labor was successful in a subsequent pregnancy in 41% of cases, compared with 83% of women who had experienced a previous vaginal delivery. Similar findings were validated by Landon et al., who described that women with previous vaginal delivery achieve a higher rate of VBAC success (87%) than women without a history of previous vaginal birth (61%). Blanchette et al. achieved a VBAC success rate of approximately 90% among women with previous vaginal delivery.

Other demographic and clinical characteristics clearly associated with successful VBAC are maternal age under 40 years, cervical dilatation greater than 4 cm at admission, birthweight less than 4000 g, whereas history of dystocia, multiple prior cesarean deliveries, alcohol and cigarette use, cephalopelvic disproportion, and obesity are associated with failure of TOL and increased maternal morbidity. However, in a study conducted to identify clinical factors that could predict failure of a TOL, Srinivas et al. showed that in a logistic regression model, which included gestational age at delivery, maternal age, maternal race, labor type, history of vaginal delivery, cephalopelvic disproportion, and prior cesarean indication, VBAC failure could not be reliably predicted.

Induction of labor has been advocated as a risk factor for uterine lesions, although studies on this topic have led to controversial results. Kayani and Alfirevic observed 4.7% of uterine lesions without a significant difference be-
between induction and spontaneous labor. Induction with prostaglandins was associated with a higher rate of failure (43%) than induction with artificial rupture and oxytocin (25%; OR 6.8, 95% CI 3.4 to 13.9). Similarly, Delaney et al observed that, although a higher maternal morbidity rate was more frequent in women undergoing induced (23%) than spontaneous labor (19%; OR 1.4, 95% CI 1.2 to 1.7), the risk of uterine rupture did not differ between groups with respective rates of 1.1% with prostaglandins induction, 0.7% with oxytocin induction, and 0.3% with spontaneous labor. Moreover, procedures in terms of blood transfusion and hysterectomy were equally performed in patients with induced (0.9%) and spontaneous (0.5%) labor. Chilaka et al obtained concordant results: no cases of uterine rupture were detected in women with successful versus failed induction after previous cesarean surgery, suggesting that induction of labor can be performed safely in women who are VBAC candidates.

Unlike the aforementioned studies, Lin and Raynor reported that induction of labor carries an increased risk of uterine injury but did not differ with regard to the induction agent. Lydon-Rochelle et al confirmed that the risk of uterine rupture is higher among patients whose labor is induced, particularly when prostaglandins are used. Another study demonstrated that women exposed to oxytocin were more likely to be affected with uterine lesion than women who were not exposed and found a relationship between doses of oxytocin and risk of uterine injury. When these studies were pooled, we observed that uterine lesions might be approximately 3 times as common among women undergoing induction of labor than among women delivering after spontaneous labor. Noteworthy, in a study with a very large sample size, the authors were unable to identify reliable predictors of uterine rupture.

Caution should be exercised in interpreting our results. By reviewing current literature, there is evidence of a substantial heterogeneity across studies concerning the selection of the study sample, definition, and management of uterine lesions and assessment of maternal complications. Moreover, women with a prior cesarean section who attempt VBAC present characteristics different from those opting for an ERCS in terms of age, body mass index, and weight gain and tend to have fewer medical problems. Such variables can represent confounding factors that can be controlled only performing randomized, controlled studies. Therefore, the absence of randomized, controlled studies in current literature does not allow driving definitive conclusion about VBAC safety. Literature also lacks of studies investigating the long-term complications, such as incontinent of urine and feces and pelvic organ prolapse, in women with previously scarred uterus and vaginal delivery in their next pregnancy. The absence of neonatal outcome data also precludes any further safety conclusion. However, the metaanalysis has the advantage to get a large sample size, which is necessary when variables under examinations are infrequent, as the case of uterine rupture.

In conclusion, our findings suggest that an increased risk of uterine disruption may result from a plan of trial of labor with respect to elective repeat cesarean delivery. However, this increase may be counterbalanced by reduction of maternal morbidity, uterine lesions, and hysterectomy when a trial of labor is successful. Thus, because in women attempting VBAC the higher morbidity rates are encountered in those who failed to achieve vaginal birth, many studies...
have concentrated on identification of risk factors for failure of a trial of labor to minimize the incidence of maternal complications. Although several studies demonstrated an association between clinical factors, maternal characteristics, and unsuccessful vaginal delivery after cesarean section, there is actually no evidence that such factors can be useful to predict outcomes in women attempting to deliver vaginally after a previous cesarean surgery.

REFERENCES