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## RISK OF UTERINE RUPTURE DURING LABOR AMONG WOMEN WITH A PRIOR CESAREAN DELIVERY

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### ABSTRACT

**Background** Each year in the United States, approximately 60 percent of women with a prior cesarean delivery who become pregnant again attempt labor. Concern persists that a trial of labor may increase the risk of uterine rupture, an uncommon but serious obstetrical complication.

**Methods** We conducted a population-based, retrospective cohort analysis using data from all primiparous women who gave birth to live singleton infants by cesarean section in civilian hospitals in Washington State from 1987 through 1996 and who delivered a second singleton child during the same period (a total of 20,095 women). We assessed the risk of uterine rupture for deliveries with spontaneous onset of labor, those with labor induced by prostaglandins, and those in which labor was induced by other means; these three groups of deliveries were compared with repeated cesarean delivery without labor.

**Results** Uterine rupture occurred at a rate of 1.6 per 1000 among women with repeated cesarean delivery without labor (11 women), 5.2 per 1000 among women with spontaneous onset of labor (56 women), 7.7 per 1000 among women whose labor was induced without prostaglandins (15 women), and 24.5 per 1000 among women with prostaglandin-induced labor (9 women). As compared with the risk in women with repeated cesarean delivery without labor, uterine rupture was more likely among women with spontaneous onset of labor (relative risk, 3.3; 95 percent confidence interval, 1.8 to 6.0), induction of labor without prostaglandins (relative risk, 4.9; 95 percent confidence interval, 2.4 to 9.7), and induction with prostaglandins (relative risk, 15.6; 95 percent confidence interval, 8.1 to 30.0).

**Conclusions** For women with one prior cesarean delivery, the risk of uterine rupture is higher among those whose labor is induced than among those with repeated cesarean delivery without labor. Labor induced with a prostaglandin confers the highest risk. (N Engl J Med 2001;345:3-8.)

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**E**ACH year in the United States, approximately 60 percent of women with a prior cesarean delivery have a trial of labor in a subsequent pregnancy. Concern persists that a trial of labor may increase the risk of maternal complications as compared with elective cesarean delivery. Such complications include uterine rupture, which is uncommon but serious and may result in hysterectomy, urologic injury, a need for blood transfusion, maternal death, and perinatal complications, including neurologic impairment and death.<sup>1-4</sup>

Population-based studies of the relation between a trial of labor and uterine rupture have had methodologic limitations and have produced inconsistent findings. A study in Nova Scotia, Canada, reported that a trial of labor was not significantly associated with uterine rupture; however, in that study, too few women had uterine rupture to provide meaningful results.<sup>2</sup> In contrast, studies in Switzerland and California demonstrated a significantly higher risk of uterine rupture among women undergoing a trial of labor than among women with elective repeated cesarean delivery.<sup>1,5</sup> However, these studies did not control for parity or the number of prior cesarean deliveries. In addition, although the rates of induction of labor among women with prior cesarean delivery have been increasing, none of these studies distinguished the risk of uterine rupture associated with a trial of labor with induction of labor from that without induction.<sup>6</sup> We used statewide linked birth-certificate and hospital-discharge data to examine the risk of uterine rupture associated with spontaneous onset of labor, induction of labor

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not involving prostaglandins, induction of labor with prostaglandins, and repeated cesarean delivery without labor among women with one prior cesarean delivery.

## METHODS

### Study Design

We conducted a population-based, retrospective cohort analysis using data obtained from the Washington State Birth Events Record Database. This data base links more than 95 percent of birth certificates in Washington State with maternal and infant records from the Comprehensive Hospital Discharge Reporting System for the hospitalization associated with delivery. The present cohort included all primiparous women who gave birth to live singleton infants by cesarean section in civilian hospitals in Washington from January 1, 1987, through December 31, 1996, and who delivered a second singleton child in Washington during the same period (a total of 20,525 women). Because a variable indicating that the women had a second cesarean section without labor ("repeat cesarean no labor") was not added to the birth certificates until 1989, we excluded the 430 women who had a second delivery before 1989. After the exclusion, 20,095 subjects remained for analysis. Demographic variables were derived from first and second birth certificates, information on payers from maternal and infant hospitalization-discharge data for the second delivery, and medical information from maternal and infant hospitalization-discharge data and birth certificates for both deliveries. The study was approved by the Human Subjects Review Committee at the University of Washington, Seattle, and the Human Research Review Board at the Washington State Department of Health, Olympia.

### Definitions

Hospitals were classified as level III (providing tertiary care, with complete perinatal services), level II (with at least 500 births per year, with board-certified obstetricians and pediatricians on staff, and providing newborn intermediate care), or level I (having a licensed obstetrical unit, with fewer than 500 births per year or without one or more level II criteria).

A delivery was classified as a repeated cesarean delivery without labor if "repeat cesarean no labor" was checked on the birth certificate and if labor-related procedure or diagnosis codes of the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM)<sup>7</sup> were not recorded on hospital-discharge forms. Labor was considered to have been induced if "induction of labor" was checked on the birth certificate or if any ICD-9-CM medical-induction procedure or diagnosis codes were recorded in hospital-discharge data. Induced labor was classified as induction of labor with prostaglandins if ICD-9-CM procedure code 96.49 was recorded on the hospital-discharge form. All other induced labor was classified as induction of labor without prostaglandins. According to these criteria, there were 6980 women who had repeated cesarean delivery without labor (34.7 percent), 1960 women who had induction of labor without prostaglandins (9.8 percent), 366 women who had induction of labor with prostaglandins (1.8 percent), and 10,789 women who had spontaneous onset of labor (53.7 percent) available for analysis. Uterine rupture was considered to have occurred if ICD-9-CM diagnosis code 665.0 or 665.1 was recorded on the hospital-discharge form.

### Statistical Analysis

To assess the risk of uterine rupture associated with spontaneous onset of labor, induction of labor without prostaglandins, and induction of labor with prostaglandins, as compared with repeated cesarean delivery without labor, we used Mantel-Haenszel rate ratios to estimate the relative risks and 95 percent confidence intervals.<sup>8</sup> Interactions between the mother's labor status at the second delivery and the type of uterine incision at the first delivery and the year of the second delivery were assessed by the likelihood-ratio test, with P values below 0.05 denoting statistical significance. No sig-

nificant interactions were found. The following variables, reported at the time of the second delivery, were examined for possible confounding effects in all analyses: maternal age; race or ethnic background; marital status; smoking status during pregnancy; presence or absence of preexisting diabetes mellitus, chronic hypertension, moderate-to-severe preeclampsia, and genital herpes; interval between the deliveries; payer; hospital level; infant birth weight and estimated gestational age; presence or absence of breech presentation; and presence or absence of placenta previa. Variables were considered to be confounders if their inclusion changed the model's relative risk for uterine rupture at the second delivery associated with any labor-status category by 10 percent or more. With this criterion, no variables were considered to confound the models.

Because misoprostol was introduced into obstetrical practice for induction of labor in Washington in 1996 and has been linked to a higher risk of uterine rupture, we compared the risk of uterine rupture associated with prostaglandin-induced labor with that associated with repeated cesarean delivery without labor, with stratification according to birth year (before 1996 or during 1996). Because prostaglandin induction may be used differently according to whether there are chronic or perinatal health conditions — which may, in turn, be independently associated with uterine rupture — we performed a secondary analysis limited to the 18,419 women without diabetes mellitus, chronic hypertension, moderate-to-severe preeclampsia, breech presentation, genital herpes, or placenta previa (91.7 percent). Because a prior vertical uterine cesarean incision may also affect a woman's risk of uterine rupture, we conducted an analysis limited to the 19,822 women (98.6 percent) without a vertical cesarean uterine incision at the first delivery. Finally, since the severity of uterine rupture cannot be determined from diagnostic codes, we examined the frequency of the diagnosis of selected postpartum complications among women with and without uterine rupture. Differences between the two groups were compared with use of the Mantel-Haenszel chi-square test. Because the frequency of postpartum complications was low, it was not possible to evaluate the relation between labor status and specific complications of uterine rupture.

## RESULTS

Demographic and perinatal characteristics at the time of the second delivery were similar among women with spontaneous onset of labor and women with no trial of labor (Table 1). Women who underwent induction without prostaglandins were more likely than women who did not have a trial of labor to deliver infants whose estimated gestational age was more than 42 weeks. Women who underwent prostaglandin induction were less likely to deliver within two years of their first delivery and more likely to deliver at a level II hospital than women who had no trial of labor. The frequency of medical conditions and complications of pregnancy varied substantially among the groups (Table 2). Women who had spontaneous onset of labor were significantly less likely than women with no trial of labor to have diabetes mellitus, chronic hypertension, preeclampsia, a breech presentation, genital herpes, or placenta previa. Women with induction without prostaglandins were significantly less likely than women who did not undergo labor to have breech presentation, genital herpes, or placenta previa. Finally, women with prostaglandin induction were significantly less likely to have breech presentation or genital herpes than women who did not undergo labor.

In our study cohort, uterine rupture complicated 4.5 second singleton deliveries per 1000 (91 women).

**TABLE 1.** CHARACTERISTICS OF SECOND DELIVERIES AMONG WOMEN WITH A PRIOR CESAREAN DELIVERY, WASHINGTON STATE, 1987 THROUGH 1996.

CHARACTERISTIC	REPEATED CESAREAN DELIVERY WITHOUT LABOR (N=6980)	SPONTANEOUS ONSET OF LABOR (N=10,789)	INDUCTION OF LABOR WITHOUT PROSTAGLANDINS (N=1960)	INDUCTION OF LABOR WITH PROSTAGLANDINS (N=366)
	number (percent)			
<b>Maternal characteristics</b>				
Age at delivery				
14–19 yr	242 (3.5)	485 (4.5)	58 (3.0)	12 (3.3)
20–24 yr	1533 (22.0)	2286 (21.2)	429 (21.9)	77 (21.0)
25–29 yr	2263 (32.4)	3283 (30.4)	609 (31.1)	121 (33.1)
30–34 yr	1620 (23.2)	2708 (25.1)	498 (25.4)	89 (24.3)
35–48 yr	1322 (18.9)	2027 (18.8)	366 (18.7)	67 (18.3)
Race or ethnic background				
White	6056 (86.8)	8949 (82.9)	1685 (86.0)	314 (85.8)
Hispanic	281 (4.0)	621 (5.8)	87 (4.4)	10 (2.7)
Asian or Pacific Islander	270 (3.9)	504 (4.7)	77 (3.9)	11 (3.0)
Black	164 (2.3)	318 (2.9)	51 (2.6)	17 (4.6)
American Indian	102 (1.5)	190 (1.8)	23 (1.2)	6 (1.6)
Other	107 (1.5)	207 (1.9)	37 (1.9)	8 (2.2)
Married	6000 (86.0)	9060 (84.0)	1712 (87.3)	312 (85.2)
Smoked during pregnancy	1150 (16.5)	1632 (15.1)	284 (14.5)	65 (17.8)
Interbirth interval				
<1 yr	86 (1.2)	125 (1.2)	19 (1.0)	4 (1.1)
1–2 yr	2167 (31.0)	3172 (29.4)	567 (28.9)	89 (24.3)
>2–3 yr	2351 (33.7)	3644 (33.8)	661 (33.7)	137 (37.4)
>3–4 yr	1280 (18.3)	2043 (18.9)	381 (19.4)	61 (16.7)
>4 yr	1096 (15.7)	1805 (16.7)	332 (16.9)	75 (20.5)
<b>Hospital characteristics</b>				
Payer				
Commercial	3936 (56.4)	5659 (52.5)	1081 (55.2)	206 (56.3)
Medicaid or uninsured	1741 (24.9)	2730 (25.3)	473 (24.1)	90 (24.6)
Managed care	1119 (16.0)	1992 (18.5)	384 (19.6)	64 (17.5)
Other	184 (2.6)	408 (3.8)	22 (1.1)	6 (1.6)
Hospital level*				
III	1673 (24.0)	2659 (24.6)	427 (21.8)	69 (18.9)
II	4516 (64.7)	7010 (65.0)	1368 (69.8)	280 (76.5)
I	791 (11.3)	1120 (10.4)	165 (8.4)	17 (4.6)
<b>Neonatal characteristics</b>				
Birth weight				
<2500 g	214 (3.1)	399 (3.7)	45 (2.3)	17 (4.6)
2500–3499 g	2956 (42.3)	4766 (44.2)	736 (37.6)	135 (36.9)
3500–3999 g	2478 (35.5)	3852 (35.7)	730 (37.2)	140 (38.3)
≥4000 g	1332 (19.1)	1772 (16.4)	449 (22.9)	74 (20.2)
Estimated gestational age				
<37 wk	434 (6.2)	672 (6.2)	80 (4.1)	26 (7.1)
37–42 wk	5350 (76.6)	7892 (73.1)	1416 (72.2)	280 (76.5)
>42 wk	439 (6.3)	861 (8.0)	226 (11.5)	33 (9.0)
Unknown	757 (10.8)	1364 (12.6)	238 (12.1)	27 (7.4)

\*Level III hospitals were tertiary care hospitals with complete perinatal services; level II hospitals had at least 500 births per year, board-certified obstetricians and pediatricians on staff, and newborn intermediate care; level I hospitals had a licensed obstetrical unit, with fewer than 500 births per year or without one or more level II criteria.

Uterine rupture occurred at a rate of 1.6 per 1000 among women with repeated cesarean delivery without labor (11 women), 5.2 per 1000 among women with spontaneous onset of labor (56 women), 7.7 per 1000 among women whose labor was induced without prostaglandins (15 women), and 24.5 per 1000 among women with prostaglandin-induced labor (9 women). Women with spontaneous onset of labor

were more likely than women who did not undergo labor to have uterine rupture (relative risk, 3.3; 95 percent confidence interval, 1.8 to 6.0) (Table 3). A greater relative risk was observed among women with induced labor without prostaglandins (relative risk, 4.9; 95 percent confidence interval, 2.4 to 9.7), and particularly those with labor induced by prostaglandins (relative risk, 15.6; 95 percent confidence interval, 8.1

**TABLE 2.** MEDICAL CONDITIONS AND SELECTED COMPLICATIONS OF PREGNANCY AT THE TIME OF THE SECOND DELIVERY AMONG WOMEN WITH A PRIOR CESAREAN DELIVERY.

CHARACTERISTIC	REPEATED CESAREAN DELIVERY WITHOUT LABOR (N=6980)	SPONTANEOUS ONSET OF LABOR (N=10,789)	INDUCTION OF LABOR WITHOUT PROSTAGLANDINS (N=1960)	INDUCTION OF LABOR WITH PROSTAGLANDINS (N=366)
		number (percent)		
Established diabetes	132 (1.9)	77 (0.7)*	25 (1.3)†	3 (0.8)‡
Chronic hypertension	155 (2.2)	115 (1.1)*	40 (2.0)†	13 (3.6)‡
Preeclampsia	66 (0.9)	34 (0.3)*	17 (0.9)†	6 (1.6)‡
Breech presentation	498 (7.1)	256 (2.4)*	8 (0.4)*	3 (0.8)*
Genital herpes	157 (2.2)	24 (0.2)*	8 (0.4)*	2 (0.5)‡
Placenta previa	108 (1.5)	43 (0.4)*	1 (0.1)*	0

\*P=0.001 for the comparison with the women who had repeated cesarean delivery without labor.

†P not significant (>0.05) for the comparison with the women who had repeated cesarean delivery without labor.

‡P=0.02 for the comparison with the women who had repeated cesarean delivery without labor.

to 30.0). For women giving birth before misoprostol became generally available in 1996, the relative risk of uterine rupture associated with prostaglandin-induced labor was 14.1 (95 percent confidence interval, 6.1 to 33.0). The risk was similar among women who gave birth in 1996 (relative risk, 12.2; 95 percent confidence interval, 3.4 to 39.6). The risk estimates for uterine rupture associated with spontaneous or induced labor were not materially changed when we excluded women with diabetes mellitus, chronic hypertension, preeclampsia, breech presentation, genital herpes, or placenta previa (data not shown). There were no uterine ruptures among the 272 women with previous vertical incisions, and the results were un-

changed when data on these women were excluded (data not shown). Women with uterine rupture were significantly more likely than women without uterine rupture to have postpartum complications (Table 4).

### DISCUSSION

In this longitudinal cohort study of 20,095 women whose first delivery of a singleton child was by cesarean delivery, a trial of labor at the second delivery was associated with a significant increase in the risk of uterine rupture. The risk of rupture was increased by a factor of approximately three in women with spontaneous labor; however, the rate of uterine rupture among these women was still quite low. The risk of uterine rupture was highest among women whose labor was induced, particularly when it was induced by prostaglandins.

Our findings are consistent with the results of two cross-sectional studies, which demonstrated increased risks of uterine rupture with a trial of labor in women with prior cesarean section.<sup>1,5</sup> A countrywide study in Switzerland, which included 92 uterine ruptures, observed a doubling of the risk among women with a trial of labor, as compared with those who underwent elective repeated cesarean delivery.<sup>1</sup> Similar risks were found in a California cohort analysis that used 1995 statewide hospital-discharge data, in which 393 uterine ruptures were reported.<sup>5</sup> One longitudinal cohort study in Nova Scotia estimated that the relative risk of uterine rupture associated with a trial of labor, as compared with elective repeated cesarean delivery, was 5.2, but only 11 women had uterine rupture, and this increase in risk was not significant.<sup>2</sup> None of those studies examined the effect of induction of labor on the risk of uterine rupture associated with a trial of la-

**TABLE 3.** INCIDENCE AND RELATIVE RISK OF UTERINE RUPTURE DURING A SECOND DELIVERY AMONG WOMEN WITH A PRIOR CESAREAN DELIVERY.\*

TYPE OF DELIVERY	NO. OF WOMEN	INCIDENCE (PER 1000)	RELATIVE RISK (95% CONFIDENCE INTERVAL)
Repeated cesarean delivery without labor	6,980	1.6	1.0
Spontaneous onset of labor	10,789	5.2	3.3 (1.8–6.0)
Induction of labor without prostaglandins	1,960	7.7	4.9 (2.4–9.7)
Induction of labor with prostaglandins	366	24.5	15.6 (8.1–30.0)

\*Incidence is expressed as the number of cases of uterine rupture per 1000 women who delivered a second singleton infant after a prior cesarean delivery. Women who had repeated cesarean delivery without labor served as the reference group.

**TABLE 4.** POSTPARTUM COMPLICATIONS OF SECOND DELIVERIES AMONG WOMEN WITH A PRIOR CESAREAN DELIVERY.\*

POSTPARTUM COMPLICATION	NO UTERINE RUPTURE (N=20,004)	UTERINE RUPTURE (N=91)
	number (percent)	
Severe posthemorrhagic anemia	958 (4.8)	10 (11.0)†
Major puerperal infection	243 (1.2)	8 (8.8)
Bladder injury	235 (1.2)	7 (7.7)
Paralytic ileus	78 (0.4)	3 (3.3)
Hysterectomy	12 (0.1)	4 (4.4)
Surgical complication‡	142 (0.7)	32 (35.2)
Maternal hospital stay >5 days	842 (4.2)	24 (26.4)
Death of infant	100 (0.5)	5 (5.5)

\*P=0.001 for the difference between the groups, except as noted.

†P=0.006.

‡Complications of anesthesia and obstetrical surgery are included.

bor. Three prior case series reported an increase in uterine rupture among women with prior cesarean delivery in whose second deliveries labor was induced by prostaglandins.<sup>9-11</sup> However, these studies did not include a comparison group of women whose second deliveries were by cesarean section without labor.

In prior studies, information about a trial of labor was based on physician-survey or hospital-discharge data alone, and labor status may have been misclassified. Information in the present study came from linked birth-certificate and hospital-discharge data — an approach that increases the accuracy and completeness of data on obstetrical diagnoses and procedures.<sup>12</sup> The use of longitudinally linked maternal data sets also allowed us to use an entire state's cohort of women with one prior cesarean delivery who had a second singleton delivery during a 10-year period; this method ensured that the number of subjects was adequate for the examination of a rare outcome. Since all levels of hospitals statewide were included, our findings represent a wide range of hospital settings.

Data derived from vital statistics and administrative records may be limited in completeness and in the accuracy of coding of obstetrical data. However, previous research has shown that 99.8 percent of cesarean deliveries are correctly classified when Washington State linked birth-certificate and hospital-discharge files are used.<sup>12</sup> Inaccuracy in the measurement of exposure is possible, however; a previous study found that only 72 percent of women with induction of labor were correctly classified in the Washington State Birth Events Record Database, and no studies have reported on the accuracy of classification of the other exposure groups.<sup>12</sup> Nonetheless, because the recording of labor

status is unlikely to depend on uterine-rupture status, any misclassification would be random and would thus lead to underestimation of the risk associated with labor. Although we could not document the accuracy of coding for uterine rupture, the observed rate of uterine rupture of 4.5 per 1000 among women with prior cesarean delivery was consistent with the results of other studies (range, 3.2 per 1000 to 6.4 per 1000).<sup>1,3,5</sup> Furthermore, the increased frequency of adverse postpartum complications among women with a diagnosis of uterine rupture suggests that this diagnosis code was clinically meaningful.

We did not have information on specific types and dosages of prostaglandin used, and therefore we could not evaluate the effects of different preparations. Although the American College of Obstetricians and Gynecologists currently advises against the use of misoprostol in women with prior uterine surgery, because of the reported increased frequency of uterine rupture, this prostaglandin analogue may have been used during 1996, the last year of our study period.<sup>11,13</sup> However, the observation that the risk of rupture associated with prostaglandin-induced labor was increased in the years before misoprostol was available indicates that this preparation alone could not have been responsible for the increased risk seen with prostaglandin use.

An increased risk of uterine rupture may be attributed to factors other than labor status at a second delivery among women with prior cesarean delivery, and these factors may also influence the decision to undertake a trial of labor. We restricted our analysis to second singleton births, eliminating the potentially confounding effects of parity, more than one cesarean delivery, and multiple gestation, all of which could have predisposed women both to a scheduled repeated cesarean delivery and to uterine rupture.<sup>14,15</sup> The results were similar when we excluded data from women with preexisting medical conditions or complications of pregnancy that might be expected to influence the mode of delivery and when we excluded data from women with prior vertical incisions.

At present, the data suggest that induction of labor increases the risk of uterine rupture among women with one prior cesarean delivery and that labor induced with use of a prostaglandin confers a greater relative risk. The overall effect of induction of labor with prostaglandins on uterine rupture is still unclear and may vary according to the preparation used, the regimen, and the degree of cervical readiness for induction.

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