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Does stage of labor at time of cesarean affect risk of subsequent preterm birth?

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Abstract

Objective—The effect of a cesarean in different stages of labor on spontaneous preterm birth (sPTB) in a subsequent pregnancy has not been extensively studied. The objective of the study was to evaluate the risk of subsequent sPTB after a first stage cesarean or second stage cesarean compared to a vaginal delivery.

Study Design—This was a planned secondary analysis of a large retrospective cohort study of women with 2 consecutive deliveries from 2005–2010. Women with prior sPTB were excluded. First stage (<10cm) and second stage cesareans (>10cm) were compared to those with a vaginal delivery. Data were obtained through chart abstraction. The primary outcome was sPTB (<37wks) in a subsequent pregnancy. Categorical variables were compared with χ^2 analyses and logistic regression was used to calculate odds and control for confounders.

Results—887 women were included (721 vaginal, 129 first stage, 37 second stage cesareans). The sPTB rate varied between groups (7.8%, 2.3%, 13.5%, $p=0.03$), respectively. When compared to a vaginal delivery, women with a first stage cesarean had a decreased risk of sPTB which remained after adjusting for confounders (aOR 0.30 [0.09–0.99], $p=0.049$). There was a non-significant increase in odds of sPTB after a second stage cesarean compared to a vaginal delivery (aOR 2.4 [0.77–7.43], $p=0.13$). Women with a second stage cesarean had a 6 fold higher odds of

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sPTB as compared to women with a first stage cesarean which remained after adjusting for confounders (aOR 5.8 [1.08–30.8], $p=0.04$).

Conclusion—Women with a full term second stage cesarean have a significantly higher than expected rate of subsequent sPTB (13.5%) compared to both the overall national sPTB rate (7–8%) and to a first stage cesarean (2.3%). As the cesarean rate continues to rise, this potential impact on pregnancy outcomes cannot be ignored.

Keywords

Cesarean delivery; preterm birth; second stage of labor

Introduction

Although the rate of preterm birth (PTB) has decreased since 2006,^{1,2} the decline has been marginal. Preterm birth remains a large public health concern and contributor to neonatal morbidity. The overall PTB rate in the United States is currently 11.7%^{1–3} with a spontaneous PTB (sPTB) rate of 7–8%.^{4–5} There are many known risks for PTB;^{1,2,6–11} however, the majority of women present without an identified risk factor.

One possible risk factor that has not been extensively studied is the effect of a prior cesarean delivery in the second stage of labor. The cervical trauma from a prolonged second stage, as well as injury of the cervix during a cesarean, are events that could alter the cervical integrity, placing women at risk for PTB in a subsequent pregnancy. For example, unintentionally incising the cervix during uterine incision or cervical extensions and lacerations during delivery may disrupt cervical integrity and compromise the cervical function for future pregnancies. This theory has been suggested by expert opinion¹² and described in case reports;^{13,14} however, the effect of a second stage cesarean delivery on PTB has not been scientifically evaluated.

Therefore, the objective of the study was to evaluate the risk of subsequent sPTB after a cesarean in the first stage of labor and second stage of labor compared to women who had a vaginal delivery. Our hypothesis was that women with a cesarean in the second stage of labor are at an increased risk of sPTB in a subsequent pregnancy as compared to women that had a vaginal delivery and compared to women that had a cesarean in the first stage of labor.

Materials and Methods

This study was a planned secondary analysis of a large retrospective cohort study designed to evaluate the impact of induction of labor on sPTB in a subsequent pregnancy. The cohort included women with two consecutive deliveries at the Hospital of the University of Pennsylvania during the years 2005–2010¹⁶. The current study uses this entire cohort to evaluate the effect that a cesarean delivery in one pregnancy has on the risk of sPTB in a subsequent pregnancy. Approval from the Institutional Review Board was obtained prior to the study.

Patient selection

Using our hospital based electronic database, we were able to obtain a list of patients that had more than one delivery between 2005 and 2010. The first pregnancy during this time period was considered their “index” pregnancy. The index pregnancy may or may not equate to the patient's first pregnancy as multiparous women were included among index pregnancies. The second pregnancy during this time period was then considered a subsequent pregnancy. Patients were included in the study only once.

As in the parent study¹⁶, this study included women whose index pregnancy was at term (≥ 37 weeks gestation) and who had a consecutive subsequent delivery ≥ 16 weeks gestational age at our institution. Women who were preterm in their index pregnancy or those with a prior preterm birth history at the time of their index pregnancy were excluded given their high a priori risk of a subsequent PTB. Women undergoing a trial of labor after cesarean were included; however, women with a planned or scheduled cesarean were excluded.

Exposure definition

The exposed group was women that had a cesarean in their index pregnancy which was subdivided into women that had a cesarean in the first stage of labor (defined as a cesarean at <10cm dilation) and women that had a cesarean in the second stage of labor (defined as a cesarean at 10cm dilation) in the index pregnancy. The unexposed group was women that had a vaginal delivery in the index pregnancy.

Outcomes Definition

The primary outcome was sPTB in a subsequent pregnancy defined as spontaneous labor and delivery or preterm premature rupture of membranes at <37 weeks gestation. The secondary outcomes were sPTB <34 weeks gestation in a subsequent pregnancy and overall PTB, which included both medically indicated PTB and sPTB <37 weeks.

Estimated gestational age at the time of delivery was based on standard obstetric dating as described in the primary paper^{16,17}. For both the index pregnancy and subsequent pregnancy, if a patient presented with unknown dating (n=12, 1.4%), an ultrasound was obtained prior to delivery to confirm if preterm or term. In those patients where an ultrasound was unable to be performed prior to delivery (n=4), a birth weight >3000g confirmed a term gestation. Gestational age was then subsequently confirmed by a pediatric exam in all patients with unknown dating.

Data collection

Data collection was through chart abstraction from the maternal and neonatal electronic medical records. Variables collected included maternal demographics as well as a full obstetrical, gynecological, medical, and social history. Labor and delivery information obtained included the lengths of the latent phase, active phase, and the second stage of labor. Delivery information was abstracted, including mode of delivery and neonatal information, for both the index and subsequent pregnancies.

Data analysis

Our analysis occurred in two stages. The first part of the analysis compared demographic data between all groups. Tests for skewness/kurtosis were performed to examine normality of continuous variables. Kruskal-Wallis tests were used to compare data which did not meet the assumptions of normality. Analysis of variance (ANOVA) was used to compare normally distributed data. Pearson chi-square and Fisher's exact tests were used to compare categorical variables as appropriate.

The second part of the analysis focused on our objective, to evaluate the risk of subsequent sPTB after a cesarean in the first stage of labor and second stage of labor compared to women who had a vaginal delivery. We used bivariate comparisons to assess for potential confounders or risk factors for the outcome, sPTB. Risk factors that were associated with the dependent variable with a significance level of $p < 0.2$ were considered candidate risk factors and/or potential confounders for multivariable modeling including included maternal age, body mass index, race, chronic hypertension, parity, prior cesarean delivery, inter-pregnancy interval, and induction of labor in the index pregnancy. We then created our multivariable model and used a backwards stepwise elimination strategy to obtain a parsimonious model. Any risk factor that impacted the effect size between exposure status and outcome by at least 15% was retained in the model as a confounder¹⁸. The confounders included in all of the final models were race, chronic hypertension, and induction of labor in the index pregnancy.

Data analysis was performed using STATA 12.0 for Windows (STATA Corporation, College Station, TX). Statistical significance was set at $p < 0.05$. The parent study had a fixed sample size of 887. The incidence of sPTB at < 37 weeks gestation among those who had a vaginal delivery during their index pregnancy (unexposed group) was 7.8%. A post-hoc power analysis was performed which showed $> 80\%$ power to detect an odds ratio of 3.6 for the association between second stage cesarean and sPTB.

Results

887 women met inclusion criteria and were evaluated. The cesarean delivery rate for the index pregnancy was 18.8% overall. Table 1 shows the demographic information for those with a vaginal delivery, those with a cesarean in the first stage of labor, and those with a cesarean in the second stage of labor in the index pregnancy. Demographic information differed among the three groups for all characteristics except the presence of gestational diabetes, pregnancy related hypertension (defined as gestational hypertension or preeclampsia), no prenatal care in the subsequent pregnancy, and the inter-pregnancy interval.

For our primary outcome, we evaluated the rate of sPTB in the subsequent pregnancy after a cesarean at different stages of labor. The subsequent sPTB rate in the overall cohort was 7.2%. We evaluated the rate of subsequent sPTB after a cesarean in the first stage of labor and the sPTB risk after a cesarean in the second stage of labor, both compared to a vaginal delivery. As noted in Table 2, the sPTB rate was significantly different across the three groups. When compared to women that had a vaginal delivery, women with a cesarean in the first stage of labor had a decreased risk of sPTB (OR 0.28 [0.09–0.91], $p = 0.03$). This

decreased risk remained after adjusting for confounders including race, chronic hypertension, and induction of labor (aOR 0.30 [0.09–0.99], $p=0.049$). There was a non-significant increase in the odds of sPTB after a cesarean in the second stage of labor compared to a vaginal delivery (aOR 2.4 [0.77–7.43], $p=0.13$). There was no difference in the gestational age of sPTB among the three groups (Table 2). We also evaluated the risk of subsequent sPTB among women with a second stage cesarean compared to women with a first stage cesarean. We found that women with a second stage cesarean had a 6.6 fold higher odds of sPTB as compared to women with a first stage cesarean (OR 6.6, [1.5–29.14], $p=0.01$). This increased odds remained after adjusting for confounders (aOR 5.8 [1.08–30.8], $p=0.04$). There were no statistically significant differences among groups with respect to overall PTB rates and sPTB rate <34 weeks (Table 2).

We then looked at the indication for cesarean delivery between those with a first stage and second stage cesarean (Table 3). Not surprisingly, the second stage cesareans were predominantly for arrest of descent or failed operative delivery (82%). The majority of the first stage cesareans were for non-reassuring fetal heart tracing (53%).

Given the high rate of sPTB in a subsequent pregnancy, we further investigated the etiology of this risk. First, we sought to explore the relationship between dilation at the time of cesarean and subsequent risk of sPTB. For this analysis we considered each centimeter (cm) of dilation as a continuous variable. We found that for each 1cm increase in dilation at time of cesarean, there was a 50% increase in the risk of sPTB (OR 1.50 [1.07–2.10], $p=0.02$). This remained after adjusting for confounders including race and induction of labor in the index pregnancy (aOR 1.46 [1.02–2.10], $p=0.04$). This linear relationship is illustrated in Figure 1 which shows the model estimates for the probability of sPTB along with the point wise 95 percent confidence intervals (CI). From these estimates, we find that the risk of sPTB after a cesarean at 6cm dilation is 2.8%, at 7cm it is 4.1%, and at 8cm dilation it is 6.0%. At 9cm dilation, the risk increases above the vaginal delivery rate (of 7.8%) to 8.7% and reaches the maximum risk of 13% after a cesarean at 10cm dilation.

Next, we evaluated the role that an extension at the time of cesarean has on the risk of sPTB. Therefore, only women who underwent a cesarean were included in this analysis. Women with an extension at the time of cesarean ($n=38$), regardless of stage of labor at which the cesarean was performed, were more likely to have a sPTB compared to women without an extension ($n=128$), (13.5% vs. 2.3%, $p=0.005$).

Comment

This is the first study to specifically evaluate the effect that a cesarean delivery in one pregnancy has on the risk of PTB in a subsequent pregnancy. We found that, when compared to a cesarean in the first stage of labor, a cesarean in the second stage of labor in one pregnancy confers a 6 fold increased odds of sPTB in a subsequent pregnancy. Additionally, both a vaginal delivery and a second stage cesarean have a higher rate of sPTB in a subsequent pregnancy compared to a first stage cesarean (7.8, 13.5% vs. 2.3%, respectively). The 13.5% risk of a sPTB in a subsequent pregnancy after a second stage cesarean is notably higher than the overall national sPTB rate of 7–8%.^{4–5}

Previous studies have suggested an increased risk of adverse outcomes after a prolonged second stage^{14,19,20} but none have specifically compared morbidity associated with a second stage cesarean compared with a vaginal delivery or a first stage cesarean. Koyama¹⁴ and Vyas¹⁹ suggested an increased risk of cervical insufficiency after a cesarean with a prolonged second stage; however, these were small case series that only evaluated women with cervical insufficiency and did not evaluate PTB risk.

Our findings suggesting an increased risk of subsequent sPTB after a second stage cesarean has biologic plausibility. While the exact mechanism of PTB is still largely unknown, premature dilation of the cervix is thought to be a cause, or perhaps a consequence, of the factors leading to PTB. Cervical trauma may be one factor that leads to the premature dilation of the cervix. The following hypotheses have both a biological and surgical component to explain potential contributions to the risk of subsequent sPTB after a second stage cesarean. Firstly, the finding that both a vaginal delivery and a second stage cesarean have a higher rate of sPTB compared to a first stage cesarean (7.8, 13.5% vs. 2.3%, respectively) indicate that there may be an inherent biological risk in achieving complete dilation, regardless of mode of delivery, or perhaps something protective about not achieving complete dilation. This could be attributed to changes in cervical stroma that occur with complete dilation that lends the cervix more susceptible to premature dilation in a future pregnancy. This hypothesis is supported by the dose response that is noted with the increased sPTB risk with each centimeter of dilation at cesarean.

Another hypothesis focuses on the surgical component contributing to the risk of subsequent sPTB. Three possibilities of intraoperative procedures that may contribute to the sPTB risk are (1) the transverse hysterotomy incision which is thought to be in the lower uterine segment but is actually at the top of the cervix, (2) the unintentional tacking up of the cervix into the hysterotomy closure, and (3) extensions down into the cervix at the time of fetal delivery. These intraoperative procedures are more common during a second stage cesarean and can lead to cervical trauma which may alter the integrity and strength of the cervix for future pregnancies. While they are exploratory findings and need to be further corroborated in future studies, the higher risk of a subsequent sPTB among women that had a cesarean with an extension further supports the fact that surgical trauma at the time of cesarean likely contributes to the risk of sPTB in a subsequent pregnancy. Even when excluding women with extensions from our analysis, there remains a statistically significant increase in the risk of sPTB after a second stage cesarean compared to a first stage cesarean (9.1% vs. 0.9%, $p=0.021$) further confirming that extensions only partly explain this elevated risk.

Our study has several strengths. It is the first study that specifically addresses the question of whether the stage of labor at which a cesarean is performed can impact future risk of sPTB. It is a large cohort study using data from one large urban hospital that minimizes practice variation during labor and delivery. Since this was a planned secondary analysis, all pertinent data on exposure, outcome, and confounders for this specific study question were obtained during the primary data collection process which included detailed chart abstraction performed solely by two investigators (LDL, AH).

Limitations of this study include the following. This was a secondary analysis and therefore the initial study was not powered for our outcome. While our post hoc power analysis found that we had > 80% power to detect an odds ratio of 3.6 for the association between second stage cesarean compared to vaginal delivery and the risk of sPTB, the observed differences in sPTB between these groups was below this level of detection (aOR 2.4 in our findings). Therefore, the lack of statistical significance for sPTB risk when comparing second stage cesarean to vaginal delivery is most likely because we are underpowered. An additional limitation is that this cohort included women with two deliveries at the same institution which may not reflect the general population. Lastly, our study has a higher rate of sPTB than is reported in the literature for multiparous women (7.8% in our study compared to ~5% in the literature). This reflects the high risk population at our institution. The baseline rate of overall PTB at our institution is 15% and the sPTB rate is 10–12%, both higher than the national average. Therefore, while the 7.8% sPTB rate for multiparous women in our study is higher than the literature, it is consistent with a reduced sPTB risk for our population. Importantly, while our results are striking, our confidence intervals are wide, most likely due to the small number of sPTB patients in our cohort. Therefore, further investigation of the impact of a second stage cesarean on risk of subsequent sPTB is warranted in future studies.

While a prior full term delivery is thought to be protective against a subsequent PTB,^{21–23} evidence is emerging of identifiable risk factors that may be contributing to the risk of subsequent PTB in these women.¹⁶ Our research further supports the multifaceted problem of PTB. Cervical trauma alone cannot contribute to the current PTB rates. It is likely that this is only one of many contributing factors that confer an increased risk of sPTB in certain women. While it is important to focus research efforts on the continued search for the etiology and treatment of PTB, it is also important to continue to identify new groups of women that may not have been previously thought to be at high risk. The women in our study that had a prior term cesarean delivery in the second stage of labor have a strikingly high risk of sPTB in a subsequent pregnancy and these findings cannot be ignored. Future studies should be aimed at surgical and therapeutic interventions and strategies that could be employed to help mitigate the risk of PTB in those women with a previous term birth.

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Figure 1.
 Spontaneous preterm birth risk per centimeter of dilation at time of cesarean
 sPTB: spontaneous preterm birth
 cm: centimeter
 CI: Confidence Interval

Table 1

Demographic information

	Vaginal (n=721)	First stage cesarean (n=129)	Second stage cesarean (n=37)	p-value
Maternal age (years) ^a	23 [19–29]	22 [19–29]	30 [24–34]	<0.001
Maternal age categories				
<18 years	8.6 (62)	10.0 (13)	0	0.007
18–35 years	84.6 (609)	81.5 (106)	78.4 (29)	
>35 years	6.8 (49)	8.5 (11)	21.6 (8)	
BMI(kg/m²) ^a	25.8 [22.1–30.6]	28.1 [24.2–33.2]	24.9 [22–26.8]	0.003
BMI categories				
Underweight	3.6 (25)	1.6 (2)	2.7 (1)	0.049
Normal weight	40.9 (284)	27.3 (35)	48.7 (18)	
Overweight	28.2 (196)	35.2 (45)	27.0 (10)	
Obese	27.3 (190)	35.9 (46)	21.6 (8)	
Gestational age at delivery (weeks) ^b	38.8 (2.5)	39.0 (1.6)	38.4 (3.3)	0.25
Race				
Black	76.7 (527)	83.7 (103)	48.6 (17)	<0.001
White	16.2 (111)	8.9 (11)	31.4 (11)	
Other	7.1 (49)	7.3 (9)	20 (7)	
Medical comorbidities				
CHTN	2.4 (17)	7.7 (10)	5.4 (2)	0.005
GDM	1.3 (9)	4.0 (5)	2.7 (1)	0.43
PRH	16.5 (119)	20.0 (26)	27.0 (10)	0.46
Parity				
Nulliparas	59.4 (428)	77.7 (101)	75.7 (28)	<0.001
Multiparas	40.6 (292)	22.3 (29)	24.3 (9)	
No prenatal care in subsequent pregnancy	46 (6.4)	9 (6.9)	0	0.27
Prior cesarean delivery	1.4 (10)	6.9 (9)	2.7 (1)	<0.001
Inter-pregnancy interval (years) ^a	1.3 [0.79–2.27]	1.4 [0.89–2.41]	1.3 [0.72–1.86]	0.09
Induction of labor in index pregnancy	66 (477)	87 (113)	86 (32)	<0.001
Birth weight in index pregnancy (g) ^b	3261.6 (±478)	3270.8 (±572)	3548.6 (±533)	0.02
NICU admission in index pregnancy	6.1 (44)	4.6 (19)	2.7 (1)	0.009

	Vaginal (n=721)	First stage cesarean (n=129)	Second stage cesarean (n=37)	p-value
Length of second stage (hours)	0.72 [0.33–1.53]	NA	3.08 [2.15–4.47]	<0.001

Presented as % (numbers) unless otherwise specified.

BMI: body mass index, CHTN: chronic hypertension, GDM: gestational diabetes, PRH: pregnancy related hypertension, NICU: neonatal intensive care unit

^a Median [Inter-quartile range]

^b Mean ($\pm$ SD)

Table 2

Primary and secondary outcomes in a subsequent pregnancy

	Vaginal (n=721)	First stage cesarean (n=129)	Second stage cesarean (n=37)	p-value
Primary outcome				
sPTB	7.8 (56)	2.3 (3)	13.5 (5)	0.03
Gestational age of sPTB (weeks) ^a	33.7 (3.9)	34.3 (1.9)	33.4 (7.1)	0.63
Secondary outcome				
Overall PTB	11.7 (84)	8.5 (11)	16.2 (6)	0.4
sPTB <34 weeks	2.9 (21)	0.8 (1)	2.7 (1)	0.4

Presented as % (numbers) unless otherwise specified.

^a Mean (SD)

Table 3

Indication for first stage and second stage cesarean delivery in the index pregnancy

	First stage cesarean n=129	Second stage cesarean n=37	p-value
Failed induction/arrest of dilation	42.6 (55)	NA	---
Non-reassuring fetal heart tracing	52.7 (68)	16.2(6)	<0.001
Arrest of descent/failed operative delivery	NA	81.8 (30)	---
Other^a	4.7 (6)	2.7 (1)	0.11

Presented as % (numbers) unless otherwise specified.

^aOther: includes maternal request and malpresentation in labor