

OBSTETRICS

Term cesarean delivery in the first pregnancy is not associated with an increased risk for preterm delivery in the subsequent pregnancy



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BACKGROUND: Prior studies have reported an increased risk for preterm delivery following a term cesarean delivery. However, these studies did not adjust for high-risk conditions related to the first cesarean delivery and are known to recur.

OBJECTIVE: The objective of the study was to determine whether there is an association between term cesarean delivery in the first pregnancy and subsequent spontaneous or indicated preterm delivery.

STUDY DESIGN: This was a retrospective cohort study of women with the first 2 consecutive singleton deliveries (2007–2014) identified through a linked pregnancy database at a single institution. Women with a first pregnancy that resulted in cesarean delivery at term were compared with women whose first pregnancy resulted in a vaginal delivery at term. Exclusion criteria were known to recur medical or obstetrical complications during the first pregnancy. A propensity score analysis was performed by matching women who underwent a cesarean delivery with those who underwent a vaginal delivery in the first pregnancy. The association between cesarean delivery in the first pregnancy and preterm delivery in the second pregnancy in this matched set was examined using conditional logistic regression. The primary outcome was overall preterm delivery <37 weeks in the second pregnancy. Secondary outcomes included type of preterm delivery (spontaneous vs indicated), late preterm delivery (34–36 6/7 weeks), early preterm delivery (<34 weeks), and small-for-gestational-age birth.

RESULTS: Of a total of 6456 linked pregnancies, 2284 deliveries were matched; 1142 were preceded by cesarean delivery and 1142 were preceded by vaginal delivery. The main indications for cesarean delivery in the first pregnancy were dystocia in 703 (61.5%), nonreassuring fetal

status in 222 (19.4%), breech presentation in 100 (8.8%), and other in 84 (7.4%). The mean (SD) gestational ages at delivery for the second pregnancy was 38.8 (1.8) and 38.9 (1.7) weeks, respectively, for prior cesarean delivery and vaginal delivery. The risks of preterm delivery in the second pregnancy among women with a previous cesarean and vaginal delivery were 6.0% and 5.2%, respectively (adjusted odds ratio, 1.46, 95% confidence interval, [CI] 0.77–2.76). In an analysis stratified by the type of preterm delivery in the second pregnancy, no associations were seen between cesarean delivery in the first pregnancy and spontaneous preterm delivery (4.6% vs 3.9%; adjusted odds ratio, 1.40, 95% confidence interval, 0.59–3.32) or indicated preterm delivery (1.6% vs 1.4%; adjusted odds ratio, 1.21, 95% confidence interval, 0.60–2.46). Similarly, no significant differences were found in late preterm delivery (4.6% vs 4.1%; adjusted odds ratio, 1.13, 95% confidence interval, 0.55–2.29), early preterm delivery (1.6% vs 1.2%; adjusted odds ratio, 1.25, 95% confidence interval, 0.59–2.67), or neonates with birthweight less than the fifth percentile for gestational age (3.6% vs 2.2%; adjusted odds ratio, 1.26, 95% confidence interval, 0.52–3.06).

CONCLUSION: After robust adjustment for confounders through a propensity score analysis related to the indication for the first cesarean delivery at term, cesarean delivery is not associated with an increase in preterm delivery, spontaneous or indicated, in the subsequent pregnancy.

Key words: linked pregnancies, mode of delivery, obstetric complications, prematurity, preterm birth, propensity score analysis, small for gestational age, subsequent delivery, vaginal delivery

Over the last 2 decades, there has been a dramatic rise in all cesarean deliveries, particularly primary cesarean deliveries, with decreasing rates of vaginal birth after cesarean.¹ In the

United States from 1996 to 2012, there was a rise in cesarean deliveries from 20.7% to 32.8%,² and as of 2017, the rate remains at 31.9%.³

Significant regional variations are observed, with some communities reporting cesarean delivery rates as high as 65%.⁴ A disturbing observation is that following cesarean delivery, studies have suggested the possibility that these women have an increased risk of subsequent preterm delivery.^{5–21}

A previous population-based cohort study that examined multiple adverse outcomes in second singleton births

found an increased risk of preterm delivery less than 37 weeks in pregnancies preceded by cesarean delivery compared with vaginal delivery (5.6% vs 4.65%; adjusted odds ratio [aOR], 1.17, 95% confidence interval [CI], 1.04–1.31) but did not differentiate between spontaneous vs indicated preterm delivery.⁵

This increased risk of preterm delivery could theoretically be driven by an increase in placental implantation abnormalities (placenta previa, placenta accreta, vasa previa, and velamentous cord insertion), which result in indicated preterm delivery to prevent the increased

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AJOG at a Glance

Why was this study conducted?

To determine the extent of the association between term cesarean delivery and preterm delivery in the subsequent pregnancy.

Key findings

In a cohort of women without medical or obstetric complications predisposing to preterm delivery and whose first pregnancy resulted in a term cesarean delivery, there is no increased risk of spontaneous or indicated preterm delivery in the subsequent pregnancy as compared with women whose first pregnancy resulted in vaginal delivery.

What does this add to what is known?

Previous studies have found a link between a first cesarean delivery and subsequent preterm delivery, but this may be a result of failing to adjust for confounding variables.

risk of maternal and fetal complications.⁶⁻¹⁵ In fact, placental implantation abnormalities, which are more common after multiple cesareans, may be implicated in as many as 8–9% of indicated preterm deliveries.¹⁶

In addition to the increased risk for indicated preterm delivery because of placental implantation abnormalities, the cesarean delivery itself may carry an inherent risk for spontaneous preterm delivery. The multifactorial nature of spontaneous preterm delivery is well documented.¹⁷⁻²⁶ It appears that a prolonged second stage,¹⁷ or more specifically a cesarean during the second stage of labor,¹⁸ may be associated with an increased risk of subsequent spontaneous preterm delivery. Possible mechanisms include prolonged pressure of the fetal head against a completely dilated cervix, incisional disruption of the muscular body of the internal cervical os, and cervical lacerations or extensions during cesarean in the second stage of labor. The aforementioned factors alone or in combination may lead to structural cervical damage, thus predisposing to subsequent spontaneous preterm delivery.¹⁹⁻²¹

If indeed there is a quantifiable risk for preterm delivery after a term singleton cesarean delivery, this would be valuable information in the shared decision making and informed consent process between patient and provider. Therefore, the objective of our study was to determine the association between term

cesarean delivery in the first pregnancy in women with no obstetrical or medical complications, known to recur in subsequent pregnancies, and preterm delivery in the second pregnancy.

Materials and Methods

This was a retrospective cohort study of women with the first 2 consecutive singleton deliveries at the Christiana Care Health System (Newark, DE) from 2007 through 2014. Data were derived through a linked pregnancy database containing maternal demographic characteristics, obstetrical factors, and labor and delivery outcomes. This longitudinal database is completed as part of a concurrent obstetrical registry and has previously been validated.²⁷

Ethics review committees of local institutional review boards at both Christiana Care Health System and Columbia University Medical Center (New York, NY) approved the protocol, and data were obtained through a data use agreement. This study was developed in conjunction with the Perinatal Research Consortium (<http://perinatalresearchconsortium.org>), which comprises 10 medical centers devoted to perinatal research.

Women with a first pregnancy that resulted in cesarean delivery at term as defined by greater than 37^{0/7} weeks' gestation were compared with women whose first pregnancy resulted in vaginal delivery at term for outcomes in the

second pregnancy. Inclusion criteria were singleton, low-risk gestations at term without medical or obstetrical complications that are known to recur such as gestational or pregestational diabetes, gestational hypertension, preeclampsia, placental abruption, preterm delivery, intrauterine growth restriction, or low birthweight, all in the first pregnancy. Patients with controlled chronic hypertension who did not develop preeclampsia were not excluded. Exclusion criteria were also multiple gestations and any other factors in the first pregnancy predisposing to preterm delivery.

Statistical analysis

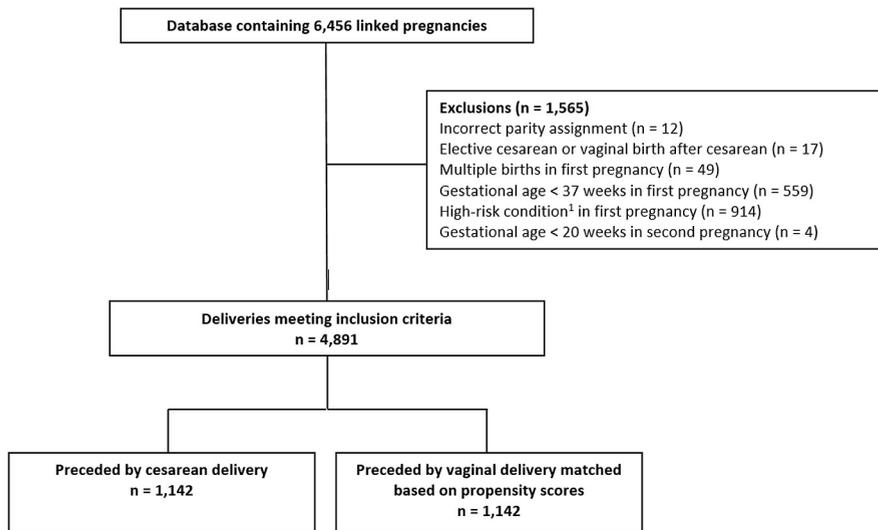
To minimize bias because of confounding, the strategy of analysis was to perform a propensity score analysis by matching women who underwent a cesarean delivery with those who underwent a vaginal delivery in the first pregnancy. Propensity score matching is used for observational data to estimate the effect of a treatment by accounting for the covariates that predict receiving the treatment.

Matching was based on risk factors after the exclusion of the aforementioned high-risk conditions known to recur. These matched risk factors included maternal age, maternal race/ethnicity, height, weight, smoking status, epidural use, presence of labor, labor induction, and epidural use, and chronic hypertension as well as all possible 2-way interactions among these risk factors.

The 2-way interaction term evaluates whether the joint effect of 2 factors is associated with the outcome more so than the effects of the 2 factors considered independently. In this study, the importance of 2-way interaction terms was evaluated based on the likelihood ratio test in a contrast of 2 nested models: one with and the other without the 2-way interaction term.

If the interaction term had a value of $P > .15$, the variable was removed. In a similar fashion, each of the interaction terms was tested, one at a time. The 2 main effects involved in a significant interaction were retained in the final model, regardless of their association with cesarean delivery. The fit of the logistic regression model was evaluated

FIGURE 1
Patient selection flow chart



¹placental abruption, gestational hypertension, pre-gestational or gestational diabetes, or small-for-gestational age birth
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based on the Hosmer-Lemeshow goodness-of-fit test. This test evaluates the extent to which the model-predicted probability of the outcome provides good approximation to the observed

data; a large *P* value indicates a good fit of the model to the data.

Once the final model was derived, the conditional probability of cesarean delivery was estimated (ie, propensity

score). Using these propensity scores, a 1:1 matched cohort of women who had a vaginal delivery in the first pregnancy was identified, with the matching based on the 5-to-1 greedy match algorithm.²⁸

This algorithm considers the predicted probability of cesarean delivery for every subject and identifies subjects whose predicted probability of vaginal delivery is the same (as that of cesarean delivery) up to the fifth decimal as a match. Once all matches are identified up to the fifth decimal precision, the algorithm identifies matches at the fourth decimal of precision in the next round. This process continues until no additional matches can be found at 1 decimal precision. In this algorithm, all women who underwent a cesarean delivery were successfully matched to women who underwent a vaginal delivery in the first pregnancy.

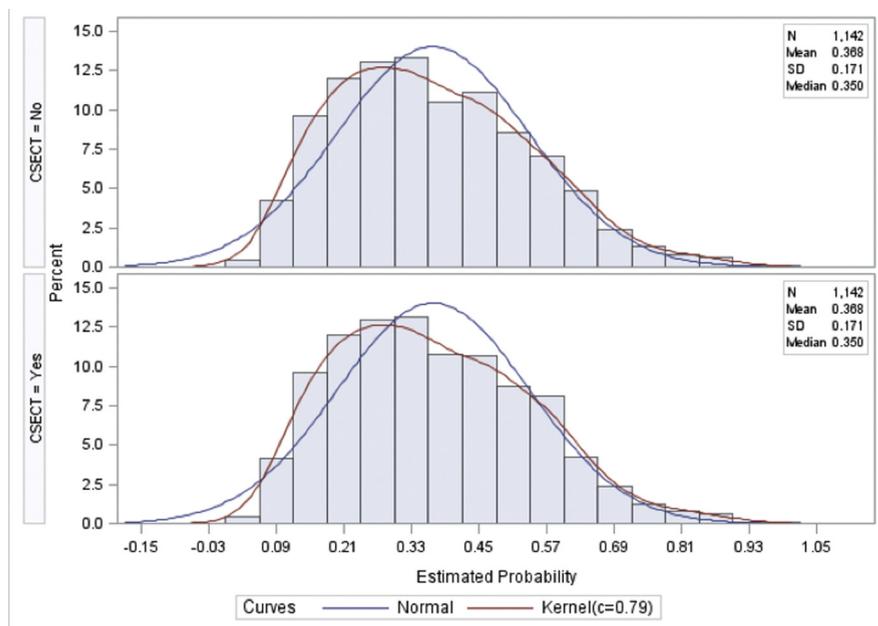
Outcomes

The association between cesarean delivery in the first pregnancy and preterm delivery in the second pregnancy in this matched set was examined using a conditional logistic regression. The primary outcome was preterm delivery at less than 37 weeks' gestation. In a subanalysis, the risks of both spontaneous and indicated preterm delivery in the second pregnancy were examined. Secondary outcomes also included late preterm delivery (between 34^{0/7} and 36^{6/7} weeks' gestation), early preterm delivery (<34 weeks' gestation), and small-for-gestational-age births (birthweight less than the fifth percentile). The norms used to define the birthweight-for-gestational-age standards were based on those of Oken et al.²⁹

Results

Of the initial cohort of 6456 linked pregnancies, the following categories were sequentially excluded: incorrect parity assignment (*n* = 12); women with an elective cesarean or a vaginal birth after a previous cesarean delivery in the first pregnancy (*n* = 17); multiple births in the first pregnancy (*n* = 49); gestational age <37 weeks in the first pregnancy (*n* = 559); any high-risk condition in the first pregnancy, including placental abruption, gestational hypertension,

FIGURE 2
Distribution of propensity scores



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pregestational or gestational diabetes, or small-for-gestational-age birth ($n = 924$); or if the gestational age at delivery in the second pregnancy was <20 weeks ($n = 4$). After all exclusions, 4891 pregnancies remained (Figure 1).

Propensity score analysis

Of the 4891 eligible pregnancies, a propensity score prediction model for term cesarean delivery in the first pregnancy was developed. This model included the following covariates in the first pregnancy that were found to be associated with the odds of cesarean delivery: gestational age in each week (modeled as a categorical variable), maternal age (modeled as a continuous variable), maternal race/ethnicity (coded as white, African American, Hispanic, Asian, and other race), smoking during pregnancy, chronic hypertension, spontaneous onset of labor, labor induction, epidural anesthesia use, rupture of membranes, prepregnancy weight, prepregnancy weight squared (modeled as a quadratic function), and height and height squared (modeled as a quadratic function).

In addition, the model also included the following 6 2-way interaction terms (all with $P < .15$): maternal race/ethnicity by smoking during pregnancy, chronic hypertension by labor induction, gestational age by spontaneous onset of labor, gestational age by labor induction, spontaneous onset of labor by labor induction, and epidural anesthesia use by labor induction. The Hosmer-Lemeshow goodness of fit of the model demonstrated an excellent fit ($P = .841$). The distribution of propensity scores among women with cesarean and vaginal deliveries is shown in Figure 2.

Maternal age and gestational age were examined for potential nonlinear associations with cesarean delivery, and it was found that these variables did not demonstrate any nonlinear associations with the odds of cesarean delivery. Therefore, a single linear term for maternal age was included, and gestational age as a categorical variable was modeled.

Once the model was fit, the predicted probabilities of cesarean delivery (ie, propensity score) were extracted for

TABLE 1

Characteristics of women whose first pregnancy resulted in a vaginal delivery or cesarean delivery

Maternal characteristics in first pregnancy	Vaginal delivery (n = 1142), n, %	Cesarean delivery (n = 1142), n, %
Maternal age, y ^a	27.5 (5.4)	27.6 (5.5)
Maternal race/ethnicity		
White	778 (68.1)	770 (67.4)
African American	196 (17.2)	203 (17.8)
Hispanic	99 (8.7)	93 (8.2)
Asian	45 (3.9)	47 (4.1)
Other	24 (2.1)	29 (2.5)
Smoking during pregnancy	121 (10.6)	125 (10.9)
Height, inches ^a	63.9 (2.9)	63.9 (2.8)
Weight, lbs ^a	189.6 (37.1)	189.5 (36.8)
Elective delivery	184 (16.1)	156 (13.7)
Epidural use	966 (84.6)	963 (84.3)
Induction of labor	508 (44.4)	530 (46.4)
Spontaneous onset of labor	1053 (92.2)	1067 (93.4)
Rupture of membranes	39 (3.4)	39 (3.4)
Chronic hypertension	27 (2.3)	26 (2.3)

^a Data are presented as mean (SD).

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every subject, and an algorithm to match subjects who underwent cesarean and vaginal deliveries in the first pregnancy were applied.²⁸ We successfully matched 1142 pregnancies that were delivered by cesarean to 1142 that were delivered vaginally in the first pregnancy. Hence, all analyses were based on 1142 matched sets (Figure 1).

Maternal characteristics of women whose first pregnancy resulted in vaginal delivery vs cesarean delivery are listed in

Table 1. As expected, the distributions of maternal and obstetrical characteristics were similar between the vaginal and cesarean delivery groups in the first pregnancy. Of the women who underwent cesarean delivery in the first pregnancy, indications for cesarean delivery are listed in Table 2. Recurring maternal medical complications or obstetrical complications predisposing to preterm delivery had previously been excluded. As such, the majority of cesarean

TABLE 2

Indications for cesarean delivery in the first pregnancy

Indication for cesarean	Frequency (n=1,142) n (%)
Dystocia	703 (61.5)
Nonreassuring fetal status	222 (19.4)
Breech presentation	100 (8.8)
Other	84 (7.4)
Information unavailable	33 (2.9)

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TABLE 3

Association between cesarean delivery in the first pregnancy and preterm delivery in the second pregnancy

Preterm delivery in second pregnancy	Mode of delivery in the first pregnancy		Propensity score matched odds ratio (95% confidence interval)
	Vaginal (n = 1142), n, %	Cesarean (n = 1142), n, %	
Gestational age at delivery, wks ^a	38.9 (1.7)	38.8 (1.8)	<i>P</i> = .512
Preterm delivery <37 weeks	59 (5.2)	69 (6.0)	1.46 (0.77–2.76)
Spontaneous preterm delivery	44 (3.9)	52 (4.6)	1.40 (0.59–3.32)
Indicated preterm delivery	15 (1.4)	17 (1.6)	1.21 (0.60–2.46)
Preterm delivery 34–36 wks	46 (4.1)	52 (4.6)	1.13 (0.55–2.29)
Preterm delivery <34 wks	13 (1.2)	17 (1.6)	1.25 (0.59–2.67)
Small-for-gestational-age births			
Birthweight <5th percentile	24 (2.2)	39 (3.6)	1.26 (0.52–3.06)

^a Data are presented as mean (SD).

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deliveries were for dystocia (n = 703; 61.5%), fetal distress (n = 222; 19.4%), and breech presentation (n = 100; 8.8%).

Outcomes are listed in Table 3. The mean gestational age at delivery for the second pregnancy was 38.9 (1.7) weeks for prior vaginal delivery and 38.8 (1.8) weeks for prior cesarean delivery, respectively. There was no difference in the odds of preterm delivery at <37 weeks in the cesarean delivery group (6.0% vs 5.2%; aOR, 1.46, 95% CI, 0.77–2.76) as well as with both spontaneous (4.6% vs 3.9%; aOR, 1.40, 95% CI, 0.59–3.32) and indicated (1.6% vs 1.4%; aOR, 1.21, 95% CI, 0.60–2.46) preterm deliveries.

Additionally, there was no difference in the odds of late preterm delivery between 34 and 36 weeks (4.6% vs 4.1%; aOR, 1.13, 95% CI, 0.55–2.29), early preterm delivery less than 34 weeks (1.6% vs 1.2%; aOR, 1.25, 95% CI, 0.59–2.67), or neonates with birthweight less than the percentile for gestational age (3.6% vs 2.2%; aOR, 1.26, 95% CI, 0.52–3.06).

Comment

Principal findings

In a cohort of women without medical or obstetrical complications predisposing to prematurity and whose first pregnancy resulted in a term cesarean delivery, there is no increased risk of

overall preterm delivery, either spontaneous or indicated, at less than 37 weeks, 34–36 weeks, or less than 34 weeks' gestation in the subsequent pregnancy, as compared with women whose first pregnancy resulted in vaginal delivery. Also, there was no increase in the rate of neonates with birthweight less than the fifth percentile in the subsequent pregnancy among those who had a prior term cesarean delivery.

Clinical implications/interpretation of the findings

Our findings suggest that women undergoing primary cesarean delivery at term in an otherwise low-risk pregnancy without predisposing medical or obstetric complications are not at increased risk for preterm delivery in the subsequent pregnancy.

This study adds to the literature on the risks associated with term cesarean delivery and can assist providers in better counseling patients regarding primary cesarean deliveries. In comparison with other studies, Kennare et al⁵ reported that second, singleton births were at increased risk of placenta previa (odds ratio [OR], 1.66, 95% CI, 1.30–2.11), placenta accreta (OR, 18.79, 95% CI 2.28–864.6), and preterm delivery (OR, 1.17, 95% CI, 1.04–1.31). They concluded that the number of primary cesareans needed to produce 1 additional adverse outcome (preterm birth) is 134.

With the rising number of cesarean deliveries, the potential contribution to prematurity becomes clinically very significant. However, as previously stated, this analysis did not differentiate between spontaneous vs indicated preterm delivery and was not adjusted for high-risk conditions that may have predisposed for cesarean delivery in the first birth, and pregnancies were not longitudinally linked.

In our study after robust adjustment for confounders and using a propensity-matched score analysis, we did not find a statistically significant risk for preterm delivery after a term cesarean. In another study, Wood et al¹⁸ reported that term cesarean delivery in the second stage of labor was associated with a subsequent increased risk of preterm delivery at less than 37 weeks (relative risk, 1.57, 95% CI, 1.43–1.73) and less than 32 weeks' gestation (relative risk, 2.12, 95% CI, 1.67–2.68) compared with vaginal delivery in a cohort of matched first and second births.

This finding could not be confirmed by Levine and Srinivas,²¹ who evaluated the effect of the length of the second stage of labor on the risk of subsequent preterm birth. While the absolute risk of spontaneous preterm birth in a subsequent pregnancy after a term cesarean delivery with a prolonged second stage of labor ≥ 3 hours was twice as high as the risk of spontaneous preterm birth after

vaginal delivery with a prolonged second stage, the results were not statistically significant (aOR, 2.08, 95% CI, 0.32–13.78). However, this could be the result of type II error.

In a more recent study published after the completion of our study, Quiñones et al¹⁷ reported an 81% increased risk of spontaneous preterm delivery in a subsequent pregnancy if there was a prolonged second stage of labor ≥ 3 hours in the first term pregnancy, with the highest risk seen in women who underwent a second-stage cesarean delivery (hazard ratio, 3.39; 95% CI, 1.09–10.49).

The latter 3 studies suggest that we need larger studies to determine whether prolonged second-stage or cesarean delivery in the second stage of labor are associated with increased preterm delivery rate in the subsequent pregnancy. In our study, our available data did not distinguish the stage of labor during which the cesarean was performed in the first pregnancy, so we were not able to conduct such an analysis.

Strengths of the study

The strengths of this study include the following: (1) the large number of patients; (2) access to a linked pregnancy database that allowed us to follow up successive pregnancies and births to the same woman; (3) robust exclusion of recurring high-risk conditions associated with the first cesarean delivery; and (4) a propensity score perfectly matched design analysis (see Figure 2), adjusting for temporally invariant confounders and additional risk factors remaining after the exclusion of the high-risk conditions of the first cesarean delivery.

Limitations of the data

This study also has a few limitations that must be taken into account. First, we excluded several subjects in the process of matching of the cohort groups in the propensity score analytic methodology. Second, the tight matching of subjects based on the mode of delivery in the first pregnancy resulted in reduced sample size, and this may have resulted in low statistical power to detect associations between the mode of delivery in the first pregnancy and preterm delivery or any

of our secondary outcomes in the second pregnancy. Of note, Kennare et al⁵ had twice the sample size of our study, but both studies demonstrate a similar trending aOR with overlapping confidence intervals, making type II error a possibility. Because our study has large numbers, if there is a link between a cesarean delivery and subsequent pregnancy outcomes, like those that we examined, this is most likely not clinically significant.

Conclusion and future research implications

After robust adjustment for confounders related to the indication for the first cesarean delivery, we found that cesarean delivery does not increase the risk of overall preterm delivery, as well as spontaneous or indicated, in a subsequent pregnancy. There does not currently appear to be an increased risk of preterm delivery inherent to the cesarean delivery itself. However, patients should be counseled regarding the increased risk of placental implantation abnormalities, which usually occurs after more than 1 cesarean in prior pregnancies. The patients in our study had only 1 cesarean and thus can explain the lack of association with subsequent indicated preterm delivery because of placental implantation abnormalities. Additionally, with the increasing number of studies revealing associations between second-stage cesarean deliveries and subsequent preterm birth,^{18–20} future directions focusing on these specific subsets of patients may help elucidate this association further. ■

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