Original Research

Maternal Morbidity Associated With Multiple Repeat Cesarean Deliveries

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OBJECTIVE: Although repeat cesarean deliveries often are associated with serious morbidity, they account for only a portion of abdominal deliveries and are overlooked when evaluating morbidity. Our objective was to estimate the magnitude of increased maternal morbidity associated with increasing number of cesarean deliveries.

METHODS: Prospective observational cohort of 30,132 women who had cesarean delivery without labor in 19 academic centers over 4 years (1999–2002).

RESULTS: There were 6,201 first (primary), 15,808 second, 6,324 third, 1,452 fourth, 258 fifth, and 89 sixth or more cesarean deliveries. The risks of placenta accreta, cystotomy, bowel injury, ureteral injury, and ileus, the need for postoperative ventilation, intensive care unit admission, hysterectomy, and blood transfusion requiring 4 or more units, and the duration of operative time and hospital stay significantly increased with increasing number of cesarean deliveries. Placenta accreta was present in 15 (0.24%), 49 (0.31%), 36 (0.57%), 31 (2.13%), 6 (2.33%), and 6 (6.74%) women undergoing their first, second, third, fourth, fifth, and sixth or more cesarean deliveries, respectively. Hysterectomy was required in 40 (0.65%) first, 67 (0.42%) second, 57 (0.90%) third, 35 (2.41%) fourth, 9 (3.49%) fifth, and 8 (8.99%) sixth or more cesarean deliveries. In the 723 women with previa, the risk for placenta accreta was 3%, 11%, 40%, 61%, and 67% for first, second, third, fourth, and fifth or more repeat cesarean deliveries, respectively.

CONCLUSION: Because serious maternal morbidity increases progressively with increasing number of cesarean deliveries, the number of intended pregnancies should be considered during counseling regarding elective repeat cesarean operation versus a trial of labor and when debating the merits of elective primary cesarean delivery. *(Obstet Gynecol 2006;107:1226–32)*

LEVEL OF EVIDENCE: II-2

The rate of cesarean delivery has substantially increased in the United States over the past few decades, with a substantial recent increase from 27.6% to 29.1% in the year 2004.[1] There are numerous contributing factors, including a decline in vaginal birth after cesarean delivery due to risk of uterine rupture, increasing maternal age, increasing rates of labor induction, decreased use of operative vaginal delivery, and medical-legal concerns.[2] Some have even advocated primary cesarean delivery.[3] Argu-

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ments in favor of increased cesarean rates include improved awareness of the risks of trial of labor after previous cesarean delivery, patient autonomy, and the relative safety of cesarean deliveries in modern obstetrics.[3–5]

Although repeat cesarean deliveries may be associated with serious morbidity, they account for only a portion of abdominal deliveries and are often overlooked when evaluating morbidity associated with cesarean delivery. Indeed, the increased risks of placenta previa and placenta accreta for pregnancies subsequent to elective primary or repeat cesarean delivery are issues of major concern that are difficult to quanitate.[6] Few studies have directly assessed the risk of repeat cesarean deliveries, and those have been conducted in a relatively small number of women.[7–12] Therefore, our objectives were to 1) estimate whether maternal morbidity is increased with increasing number of cesarean deliveries and 2) to estimate the risks of placenta previa and placenta accreta associated with increasing number of cesarean deliveries.

MATERIALS AND METHODS

The study consisted of a prospective observational cohort of women undergoing cesarean delivery from 1999 through 2002 at 19 academic medical centers within the National Institute of Child Health and Development Maternal-Fetal Medicine Units Network. The methodology of the cohort has been described in detail[13] and includes 4 years of enrollment of women undergoing repeat cesarean deliveries and 2 years of enrollment of all women undergoing primary cesarean deliveries. Important features of the protocol included prospective daily ascertainment of cesarean deliveries in all participating hospitals and direct abstraction of data from medical records by trained study nurses. The study was approved by the human subjects committee at each participating center.

Maternal outcome and surgical complications for women undergoing increasing number of cesarean deliveries were compared with those undergoing primary cesarean deliveries. This analysis focused on the cohort of women who had cesarean delivery without labor because labor is a major potential confounding variable for maternal (and fetal) morbidity. Primary outcome variables included the occurrence of placenta accreta, placenta previa, bladder, bowel or ureteral injury, the need for hysterectomy, blood products, admission to the intensive care unit, and ventilator support, and the occurrence of deep venous thrombosis, pulmonary embolism, postpartum endometritis, wound infection, wound dehiscence, ileus, and maternal death.

All inpatient medical records were abstracted through 6 weeks postpartum. However, patients were not directly contacted to determine whether they had additional complications that were treated in institutions other than where their cesarean deliveries were performed. Thus, some late-onset complications, such as thrombosis or ureteral injury, may not have been ascertained.

Postpartum endometritis was defined as a clinical diagnosis of puerperal infection in the absence of findings suggesting a nonuterine source of infection. *Placenta accreta* was defined as the placenta being adherent to the uterine wall without easy separation. This definition included *placenta accreta*, *increta*, and *percreta*, based on histologic findings, or based on clinical findings if hysterectomy was not performed. *Cystotomy* included elective and accidental cases, which were not distinguished in the database. Bowel injuries, ureteral injuries, and ileus were reported by the physician based on clinical impression. Details regarding specifics (eg, type of bowel injury) were not ascertained.

To test for trend among women with increasing number of cesarean deliveries, the Cochran-Armitage trend test was used for binomial outcomes and the Jonckheere-Terpstra test was used for continuous outcomes.[14,15] To test for any baseline differences among the groups, the χ^2 test was used for categorical outcomes, and the Kruskal-Wallis test was used for continuous outcomes. Odds ratios and 95% confidence intervals were calculated for the risk of adverse outcomes for each successive cesarean delivery compared with the risk for a primary cesarean delivery. The risk of comorbidities by placenta accreta or hysterectomy status was compared by using the χ^2 or Fisher exact test, as appropriate. Multivariable logistic regression analysis was performed to adjust for potential confounding variables contributing to adverse maternal outcome. Potential confounding variables included race, maternal age, insurance status, prenatal care, maternal disease, and gestational age at delivery. Statistical analyses were performed with SAS 8.2 (SAS Institute, Cary, NC) statistical software

RESULTS

There were 378,063 births during the study period, including 83,754 cesarean deliveries. Of these, 30,132 occurred without labor and had data on previous pregnancies and detailed outcome data for this pregnancy. These made up the study cohort. Demographic information and patient characteristics, according to the number of cesarean deliveries, are shown in Table 1. Overall, the cohort was 45% white,

Table 1. Demographic Characteristics and Delivery Outcome of Women Who Had Cesarean Deliveries Without Labor

Characteristic	First CD*	Second CD	Third CD	Fourth CD	Fifth CD	≥ 6 CD	$P^{\dagger}$
No.	6,201	15,808	6,324	1,452	258	89	–
Race or ethnic group							
White (%)	52.6	45.7	37.1	41.0	53.8	47.7	< .001
African American (%)	27.0	22.0	23.4	27.7	28.9	38.6	
Hispanic (%)	18.7	30.1	38.1	30.2	16.1	12.5	
Other or unknown (%)	1.7	2.2	1.5	1.1	1.2	1.1	
Prenatal care (%)	97.5	98.9	98.5	98.9	96.5	93.3	.03
Singleton pregnancy (%)	88.7	97.5	98.4	98.4	99.6	97.8	< .001
Smoker during pregnancy (%)	15.0	11.3	12.8	16.5	18.6	24.7	.18
Maternal disease (%)‡	23.5	23.9	22.9	25.1	26.4	33.7	.38
Maternal age at delivery (y, mean ± SD)	28.1 ± 6.6	29.5 ± 5.8	30.1 ± 5.4	31.3 ± 5.3	33.1 ± 5.3	34.2 ± 5.0	< .001§
Gestational age at delivery (wk, mean ± SD)	36.0 ± 4.2	38.3 ± 2.5	38.3 ± 2.1	38.1 ± 2.2	37.9 ± 2.5	37.5 ± 2.5	< .001§
Delivery at < 37 weeks (%)	44.7	14.6	12.8	16.7	19.1	31.8	< .001

CD, cesarean delivery; SD, standard deviation.
* Primary cesarean delivery.
† *P* values are from Mantel-Haenszel χ^2 test for trend unless otherwise indicated.
‡ Diabetes, chronic hypertension, asthma, seizure disorder, thyroid disease, renal disease, or connective tissue disease.
§ These *P* values are from the Kruskal-Wallis sum test.

24% African American, 29% Hispanic, and 1.9% other ethnicity. Forty-seven percent had private insurance, 98.5% underwent at least one prenatal visit, and 96% were singleton pregnancies. Data were not collected regarding the total number or timing of prenatal visits. Women with higher order multiple cesarean deliveries were older and more likely to be African American and to have no private health insurance than those having fewer cesareans (Table 1; $P < .05$ for each).

Table 2 depicts maternal morbidity according to numerical order of the most recent cesarean delivery. Increased risks of placenta accreta, hysterectomy, transfusion of 4 units or more of packed red blood

Table 2. Maternal Morbidity of Women Who Had Cesarean Deliveries Without Labor

Morbidity	First CD*	Second CD	Third CD	Fourth CD	Fifth CD	≥ 6 CD	$P^{\dagger}$
No.	6,201	15,808	6,324	1,452	258	89	–
Placenta accreta	15 (0.24)	49 (0.31)	36 (0.57)	31 (2.13)	6 (2.33)	6 (6.74)	< .001
Hysterectomy	40 (0.65)	67 (0.42)	57 (0.90)	35 (2.41)	9 (3.49)	8 (8.99)	< .001
Any blood transfusion	251 (4.05)	242 (1.53)	143 (2.26)	53 (3.65)	11 (4.26)	14 (15.73)	.61
Blood transfusion ≥ 4 units	65 (1.05)	76 (0.48)	49 (0.77)	23 (1.59)	6 (2.33)	9 (10.11)	< .001
Cystotomy	8 (0.13)	15 (0.09)	18 (0.28)	17 (1.17)	5 (1.94)	4 (4.49)	< .001
Bowel injury	7 (0.11)	9 (0.06)	8 (0.13)	5 (0.34)	0 (0.00)	1 (1.12)	.02
Ureteral injury	2 (0.03)	2 (0.01)	1 (0.02)	1 (0.07)	1 (0.39)	1 (1.12)	.008
Placenta previa	398 (6.42)	211 (1.33)	72 (1.14)	33 (2.27)	6 (2.33)	3 (3.37)	< .001
Ileus	41 (0.66)	71 (0.45)	43 (0.68)	13 (0.90)	4 (1.55)	3 (3.37)	.01
Postoperative ventilator	62 (1.0)	33 (0.21)	15 (0.24)	10 (0.69)	2 (0.78)	1 (1.12)	< .001
Intensive care unit admission	115 (1.85)	90 (0.57)	34 (0.54)	23 (1.58)	5 (1.94)	5 (5.62)	.007
Operative time (min)	50.6 (24.0)	54.9 (23.2)	60.7 (25.6)	64.5 (32.7)	67.9 (32.6)	79.9 (53.4)	< .001‡
Hospital days	5.6 (7.2)	3.9 (4.2)	3.8 (4.0)	4.2 (5.2)	4.1 (5.0)	5.5 (7.8)	< .001‡
Wound infection	95 (1.53)	148 (0.94)	97 (1.53)	19 (1.31)	9 (3.45)	3 (3.37)	.09
Endometritis	371 (5.98)	404 (2.56)	178 (2.81)	43 (2.96)	4 (1.55)	6 (6.74)	< .001
Wound dehiscence	23 (0.37)	17 (0.11)	10 (0.16)	3 (0.21)	2 (0.78)	0	.18
Deep venous thrombosis	17 (0.27)	24 (0.15)	9 (0.14)	3 (0.21)	0	1 (1.12)	.42
Pulmonary embolus	13 (0.21)	18 (0.11)	5 (0.08)	4 (0.28)	1 (0.39)	1 (1.12)	.85
Reoperation	26 (0.42)	35 (0.22)	16 (0.25)	6 (0.41)	1 (0.39)	3 (3.37)	.57
Maternal death	12 (0.19)	11 (0.07)	3 (0.05)	1 (0.07)	0	0	.02

CD, cesarean delivery.
Data are presented as n (%).
* Primary cesarean delivery.
† *P* values are from Cochran-Armitage test for trend unless otherwise indicated.
‡ These *P* values are from Spearman rank correlation test.

cells, cystotomy, bowel injury, ureteral injury, ileus, intensive care unit admission, and longer operative time were seen with an increasing number of cesarean deliveries. After the first cesarean, increased risk of placenta previa, need for postoperative (maternal) ventilator support, and more hospital days were seen with increasing number of cesarean deliveries. The risk of placenta accreta reached 2% in women having their fourth cesarean delivery and was over 6% in those with 6 or more procedures. Nine percent of women having 6 or more cesarean deliveries required hysterectomy. Other morbidity, including wound dehiscence, deep venous thrombosis, pulmonary embolus, the need for reoperation, and death, was not increased in women with increasing number of cesarean deliveries. Endometritis was more common among women undergoing primary cesarean delivery than in women undergoing a second to fifth cesarean delivery without labor. The rate of maternal death was higher among women undergoing primary cesarean than all others, but the two deaths that could potentially be attributed to the cesarean delivery occurred in women undergoing a repeat (second) cesarean delivery.

The odds ratios for having placenta accreta and hysterectomy for each successive cesarean delivery compared with the risks for primary cesarean delivery are shown in Table 3. Women having their fourth or more cesarean delivery had a 9- to 30-fold increased risk of placenta accreta and a 4- to 15-fold higher risk of hysterectomy. Of the 216 hysterectomies, 195 were performed during the same surgery as the cesarean delivery and 21 at a second surgery.

There was a statistical association between increased number of cesarean deliveries and placenta previa in our cohort after the second cesarean delivery (Table 2). However, in individuals with placenta previa, the risk of placenta accreta dramatically increased with increased number of prior cesareans (table 4). The risk of placenta accreta increased with increasing number of cesarean deliveries, even in women without placenta previa.

Maternal morbidity was substantially increased in all women with placenta accreta and/or hysterectomy compared with those not having placenta accreta and/or hysterectomy (Tables 5 and 6). Among women with placenta accreta, the risk of hysterectomy increased with increasing number of cesarean deliveries.

To assess for the influence of possible confounding variables, a logistic regression model was generated. After controlling for race, maternal age, marital status, insurance status, number of fetuses, maternal disease, and prenatal care, all of the significant associations between maternal morbidities and increasing number of cesarean deliveries remained similar and statistically significant. For example, the unadjusted odds ratio (OR) for placenta accreta with increasing number of cesarean deliveries as a continuous variable is 1.949 (95% confidence interval [CI] 1.724–2.204). The adjusted OR is 1.750 (95% CI 1.533–1.997). For hysterectomy, the unadjusted OR is 1.752 (95% CI 1.569–1.956), and the adjusted OR is 1.594 (95% CI 1.418–1.793).

There were too many medical centers (n = 19) included in the study to include them all in a model to address the potential effect of center-to-center variation. However, the three centers contributing the most patients were included in a multivariable model. Again, all of the associations between maternal morbidities and increasing number of cesarean deliveries remained similar and statistically significant. Thus, it is unlikely that center-to-center variation influenced our results.

DISCUSSION

Serious maternal morbidity increases with increasing number of cesarean deliveries. The majority of this risk is attributable to that associated with placenta accreta and/or the need for hysterectomy. Placenta

Table 3. Odds Ratios With 95% Confidence Intervals for Placenta Accreta and Hysterectomy by Number of Cesarean Deliveries Compared With First Cesarean Delivery

Cesarean Delivery	Accreta [n (%)]	OR (95% CI)	Hysterectomy [n (%)]	OR (95% CI)
First*	15 (0.2)	–	40 (0.7)	–
Second	49 (0.3)	1.3 (0.7–2.3)	67 (0.4)	0.7 (0.4–0.97)
Third	36 (0.6)	2.4 (1.3–4.3)	57 (0.9)	1.4 (0.9–2.1)
Fourth	31 (2.1)	9.0 (4.8–16.7)	35 (2.4)	3.8 (2.4–6.0)
Fifth	6 (2.3)	9.8 (3.8–25.5)	9 (3.5)	5.6 (2.7–11.6)
≥ 6	6 (6.7)	29.8 (11.3–78.7)	8 (9.0)	15.2 (6.9–33.5)

OR, odds ratio; CI, confidence interval.
* Primary cesarean delivery.

Table 4. Placenta Previa and Placenta Accreta by Number of Cesarean Deliveries

Cesarean Delivery	Previa	Previa*:Accreta† [n (%)]	No Previa‡:Accreta† [n (%)]
First§	398	13 (3.3)	2 (0.03)
Second	211	23 (11)	26 (0.2)
Third	72	29 (40)	7 (0.1)
Fourth	33	20 (61)	11 (0.8)
Fifth	6	4 (67)	2 (0.8)
≥ 6	3	2 (67)	4 (4.7)

* Percentage of accreta in women with placenta previa.
† Increased risk with increasing number of cesarean deliveries; $P < .001$.
‡ Percentage of accreta in women without placenta previa.
§ Primary cesarean.

Table 5. Placenta Accreta and Comorbidity

Morbidity	No Accreta (%)	Accreta (%)	*P*
Cystotomy	0.15	15.4	< .001
Ureteral injury	0.02	2.1	< .001
Pulmonary embolus	0.13	2.1	.001
Ventilator	0.3	14	< .001
Intensive care unit	0.8	26.6	< .001
Reoperation	0.26	5.6	< .001
Endometritis	3.34	3.50	.81

Table 6. Hysterectomy and Comorbidity

Morbidity	No Hysterectomy (%)	Hysterectomy (%)	*P*
Cystotomy	0.14	12.04	< .001
Ureteral injury	0.01	2.31	< .001
Pulmonary embolus	0.13	1.85	< .001
Ventilator	0.32	12.5	< .001
Intensive care unit	0.74	23.15	< .001
Reoperation	0.21	11.6	< .001
Endometritis	3.33	4.17	.50

accreta was present in more than 2% of patients having their fourth and in 6.7% of those undergoing their sixth or greater cesarean delivery. Almost 1 in 40 (2.4%) women undergoing their fourth cesarean delivery required hysterectomy (compared with 0.65% of primary cesareans); the risk increased to 1 in 11 (9%) having their sixth or greater procedure. In the absence of placenta accreta or the need for hysterectomy, there still was an association between maternal morbidity and increasing cesarean delivery number for all morbidities other than deep venous thrombosis. Thus, even in the absence of placenta previa or placenta accreta, women undergoing multiple repeat cesarean deliveries cannot be entirely reassured. Other surgical morbidity, including blood transfusion of 4 units or more, cystotomy, bowel injury, ureteral injury, previa, ileus, the need for (maternal) postoperative ventilation, intensive care unit admission, operative time, and days of hospitalization, also was increased with increasing number of cesarean deliveries.

Previous studies examining the risk of surgical morbidity with repeat cesarean delivery have reported mixed results. Some have reported no association.[10,11] We speculate that this discrepancy may be due to the relatively small number of subjects included in those cohorts. We performed a PubMed search of papers written in English from January 1980 to August 2005, using the keywords "cesarean delivery," "multiple," and "complications." In the largest previously reported cohort of repeat cesarean deliveries, including 3,191 cases from Saudi Arabia (1,585 with 3 or more cesarean deliveries), Makoha and colleagues also noted increased maternal morbidity, including placenta previa, placenta accreta, hysterectomy, adhesions, bladder injury, postoperative hemoglobin deficit, and need for blood transfusion with increasing number of cesarean deliveries.[12] As with our cohort, most morbidity was associated with placenta accreta and hysterectomy.

Although repeat cesarean delivery was associated with increased maternal morbidity, outcomes were good in most women undergoing these procedures. Maternal death was rare, and in only 2 cases (in women having their second cesarean delivery) could it potentially be attributable to cesarean delivery morbidity. Thus, there does not appear to be an absolute threshold number of cesarean deliveries beyond which patients should be unequivocally counseled to forgo future pregnancies. Others also have not definitively delineated a threshold for number of cesarean deliveries.[11,12] On the other hand, our study did not have enough power to adequately evaluate whether rare but serious events such as death were increased with increasing number of cesarean deliveries. Indeed, the rates for rare complications are estimates, especially in women with 4 or more cesar-

ean deliveries. Nonetheless, there was a substantial increase in the risk for several morbidities, including placenta accreta, cystotomy, and need for hysterectomy or intensive care unit admission with the fourth or greater cesarean delivery. Women should be counseled regarding the progressive increase in the risk for meaningful morbidity with repeat cesarean deliveries.

The rate of placenta previa (after the first cesarean delivery) increased with increasing number of cesarean deliveries in our cohort. This is similar to others who reported an association between repeat cesarean deliveries and placenta previa.[12,16] However, Hershkowitz and colleagues[17] found no association between many cesarean deliveries and placenta previa. Different results may be attributable to differences in patient population because the Hershkowitz study included relatively few women having their fourth or greater cesarean delivery.[17] We cannot comment on the relative effects of parity, a known risk factor for placenta previa,[18] because our cohort included only cesarean deliveries, as opposed to all deliveries.

Our results confirmed the strong association between placenta accreta and increasing number of cesarean deliveries in women with placenta previa.[12,19] In cases of placenta previa, the risk of placenta accreta was 40% for those having their third cesarean delivery and over 60% for the fourth or greater cesarean delivery. These results are similar to previous studies.[12,19] However, placenta accreta occurred in only 11% of our patients having their second cesarean delivery with a placenta previa. This is substantially less than the risk of 24% that has been generally accepted.[19] The subjective nature of the diagnosis in some cases may account for differences among studies. Also, the current study includes substantially more women with placenta previa and prior cesarean delivery than previous investigations. Finally, because the data are more recent, they may more accurately reflect current management of placenta previa in the setting of prior cesarean delivery. Another recent cohort found no placenta accretas in 23 women with placenta previa and one prior cesarean delivery.[12]

The large percentage of cases performed by resident physicians may introduce bias toward unfavorable outcomes and is a potential limitation of the study. It is not possible to evaluate this issue since participation of resident physicians in each case was not assessed. The relatively large proportion of "high risk" cases seen in these referral centers is an additional potential source of bias toward worse outcomes. Conversely, the inclusion of cases from mostly tertiary care, large, urban hospitals may introduce bias toward more favorable outcomes because of the availability of blood banks and consultant subspecialty surgeons. Accordingly, results may not be generalizable to smaller rural hospitals, and our data likely underestimate the actual risk in smaller hospitals without special services. Another possible limitation was our use of a clinical definition for placenta accreta. However, histologic diagnosis of placenta accreta was not always possible because not all women given the diagnosis of placenta accreta underwent hysterectomy. Finally, obesity was a potential confounder. As expected with increasing parity and age, obesity was more common in women with increasing number of cesarean deliveries. Although obesity is a known risk factor for cesarean morbidity,[20] it was unlikely to account for the most serious morbidities in the study, such as placenta accreta. Data regarding obesity were incomplete, with 30% of patients having missing values. Thus, it was not possible to adequately assess the effects of obesity in a multivariable model.

A major strength of the study was its size. This cohort is substantially larger than previous investigations, including over 6,000 women with third cesarean deliveries, almost 1,500 with fourth cesarean deliveries, and 347 with fifth or greater cesarean deliveries. The cohort also included 723 women with placenta previa. Other strengths include an inclusive prospective cohort, multicenter participation, recent data reflecting current management of placenta accreta, and the use of trained obstetric research nurses for data collection.

We believe that our data have important implications for counseling patients regarding elective cesarean delivery and trial of labor after previous cesarean delivery. The cesarean delivery rate in the United States is currently over 29% and continues to rise.[1] We estimate that over 80,000 women in the United States had their fourth or more cesarean delivery last year, a number that will certainly increase. Although the general safety of cesarean delivery is well established,[3–5] morbidity from multiple procedures may not be taken into account. It is important to consider not only the morbidity from the initial cesarean delivery, but that from subsequent pregnancies as well. Thus, women planning large families should consider the risks of repeat cesarean deliveries when contemplating elective cesarean delivery or attempted vaginal birth after cesarean delivery. Our data also will facilitate counseling of women with placenta previa and prior cesarean deliveries regarding their risks of placenta accreta.

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APPENDIX

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