Optimal Timing of Delivery in Women with Higher Order Cesareans: A Cohort Study

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Abstract

Objective   To evaluate whether a planned early term delivery or a planned 39-week delivery is associated with differences in perinatal outcomes in women undergoing a higher order cesarean (HOC).

Study Design   This cohort study included women with singleton gestations with a history of three or more prior cesareans who delivered at one of two urban tertiary care hospitals. One center routinely delivered HOC at 39 weeks' gestation and the other at 37 weeks. Maternal and neonatal morbidities were compared using bivariable and multivariable analyses.

Results   The policy of 37-week delivery was associated with a decrease in unscheduled deliveries (15.3 vs. 41.1%; $p < 0.001$). Planned delivery at 37 weeks was associated with a decreased incidence of composite maternal morbidity (1.6 vs. 7.9%; $p = 0.002$) and 5-minute Apgar score less than 7 (0.4 vs. 6.4%; $p < 0.001$), but these differences were not significant after controlling for potential confounders (adjusted odds ratio [aOR]: 0.30, 95% confidence interval [CI]: 0.08–1.17; aOR: 0.13, 95% CI: 0.01–1.30, respectively). There were no other differences in perinatal outcomes.

Conclusion   Compared with planned delivery at 39 weeks, a policy of planned delivery at 37 weeks was associated with a reduction in unscheduled deliveries, but there were no measured differences in perinatal outcomes.

Keywords
► higher order cesarean
► multiple cesareans
► timing of delivery
► obstetric complications

The rate of cesarean delivery in the United States has risen steadily for 20 years, from 20.1% in 1996 to 32.2% in 2014.[1] This trend is the result of both a large increase in the rate of primary cesarean delivery and a decrease in the number of women attempting vaginal birth after cesarean (VBAC); currently approximately 90% of women in the United States will opt for repeat cesarean delivery rather than VBAC.[2] As a result, prior cesarean delivery has become one of the most common indications for cesarean delivery.[2]

An increased number of prior cesarean deliveries is associated with an increase in maternal operative risks.[3,4] Both meta-analyses and observational studies have shown that, compared with primary cesareans, higher order cesareans (three cesarean deliveries or more) are associated with increased frequencies of intraoperative complications and that the risk of complications increases with each subsequent cesarean.[5–8] These complications include an increase in severe intraperitoneal adhesions,[6–10] excessive blood loss,[7,11] and bowel and bladder injuries.[7,12,13] Lastly, there is a clear link between the number of prior cesareans and the risk of peripartum hysterectomy, which rises from 0.65% for the first cesarean delivery to 8.99% for the sixth.[7] In addition,

higher order cesarean delivery is associated with an increased operative time.[6,10,13,14] While evidence is mixed regarding neonatal effects of prolonged operative time, a longer incision to delivery interval has been associated with an increased frequency of neonatal hypoxic morbidity.[14,15] An unscheduled presentation due to labor only serves to compound these risks.

One intervention to potentially decrease these maternal and neonatal morbidities in the setting of a higher order cesarean delivery is to reduce the incidence of an unscheduled delivery by planning for an early term delivery. The risks of an unscheduled delivery, however, must be weighed against the neonatal risks associated with early term delivery.[16] There is no clear guidance about delivery timing for women with three or more prior cesareans. Therefore, the goal of this study is to determine whether a policy of planned delivery at early term (37 weeks) or a policy of planned delivery at 39 weeks is associated with differences in maternal and neonatal outcomes.

Materials and Methods

This was a retrospective cohort study of women with singleton gestations who delivered at one of two large academic urban tertiary care hospitals. Women were included in the study if they had undergone three or more prior cesarean deliveries, irrespective of whether their cesarean was planned or unplanned. Women were excluded from this study if they had multiple gestations, known major fetal anomalies, known abnormal placentation (placenta previa or placenta accreta), a history of prior classical cesarean, or a prior cavity-entering uterine surgery.

One center routinely delivers higher order cesareans at 39 weeks' gestation, and electronic medical records from that institution were available and reviewed between January 1, 2010, and July 1, 2016. The other center routinely delivers higher order cesareans at 37 weeks' gestation after either confirmation of fetal lung maturity by amniocentesis or administration of antenatal steroids. Electronic medical records from that institution were available and reviewed between June 1, 2005, and June 1, 2016. Both centers used contemporary American College of Obstetricians and Gynecologists criteria to determine the gestational age throughout the study period.[17] Cesareans in both centers were performed by an attending obstetrician assisted in the center with routine 37-week deliveries by either a resident physician or a second attending obstetrician and in the center with routine 39-week deliveries by either a resident physician or a surgical assistant. As perinatal outcomes are similar irrespective of the type of surgical assistant involved in higher order cesareans,[18] this was not considered a potential confounder.

Records from both institutions were then reviewed for maternal clinical information, including maternal age, race/ethnicity, gravidity, parity, body mass index (BMI) at delivery, number of previous cesareans, concomitant major medical problems, indication for delivery (i.e., scheduled versus unscheduled), and gestational age at delivery. Electronic records were also reviewed for maternal operative compli-

cations such as maternal death, cystotomy, bowel injury, maternal intensive care unit (ICU) admission, peripartum hysterectomy, postpartum hemorrhage (defined as an estimated blood loss [EBL] > 1,000 mL), transfusion, and total operative time. During the study period, at both centers, EBL was assessed by the attending obstetrician in concert with the anesthesiologist present. A composite maternal adverse outcome consisting of cystotomy, bowel injury, hysterectomy, need for a blood transfusion, and maternal ICU admission was generated. Neonatal outcomes were also abstracted, including 5-minute Apgar score, neonatal intensive care unit (NICU) admission, NICU length of stay (if NICU admission occurred), and neonatal death. During the study period, NICU admission was decided by the attending neonatologist either present at delivery or postpartum due to clinical concerns of fetal or neonatal distress. Markers of neonatal and maternal morbidity and mortality were then compared, stratified by delivery timing policy in bivariable analyses using chi-square or Fisher's exact tests for categorical variables or Mann Whitney–U tests for continuous variables. Multivariable logistic regressions were performed to determine whether the delivery timing policy was independently associated with each of the adverse outcomes identified to be different between the sites. Variables were entered in each multivariable model if they demonstrated an association with site at a $p < 0.05$ level in the univariable analysis.

All analyses were performed using Stata version 14.0 (StataCorp, College Station, TX). All tests were two-tailed and an α of 0.05 was used to determine statistical significance. The study was reviewed and approved by the Institutional Review Boards at Northwestern University and the Mount Sinai Hospital with a waiver of informed consent. Data were deidentified prior to analysis.

Results

During the study period, 440 women met inclusion criteria: 190 (43.2%) women from the institution with a policy of delivery at 39 weeks and 250 (56.8%) women from the institution with a policy of delivery at 37 weeks. Patient demographic, obstetric, and medical characteristics are shown in ►Table 1. Women who delivered at the center with a policy of early term delivery were significantly older, more parous, more likely to be a non-Hispanic white, had a lower delivery BMI, less likely to have medical comorbidities, and had a higher number of prior cesarean deliveries compared with women who delivered at the center with a policy of delivery at 39 weeks. Delivery was more likely to require a nonlow transverse incision in women at the center with a policy of delivery at 37 weeks compared with 39 weeks.

Bivariable analyses of maternal complications are given in ►Table 2. Compared with a policy of early term delivery, a policy of delivery at 39 weeks was associated with an increased frequency of requiring an unscheduled cesarean. There were no differences in the incidence of bowel injury, maternal ICU admission, or hysterectomy between the two cohorts. Cystotomy was more common in women who delivered at the hospital with a policy of 39-week delivery

Table 1 Demographic and obstetric characteristics stratified by delivery timing policy

	Policy of delivery at 39 wk, *n* = 190	Policy of delivery at 37 wk, *n* = 250	*p*-Value
Maternal age (years)	34.5 (30–38)	35.2 (32.1–38.2)	0.016
Maternal parity	3 (3–3)	4 (3–5)	<0.001
Maternal race/ethnicity			
Non-Hispanic white	81 (42.6%)	246 (98.4%)	<0.001
Non-Hispanic black	29 (15.3%)	4 (1.6%)	
Asian	2 (1.1%)	0	
Hispanic	43 (22.6%)	0	
Other/not applicable	35 (18.4%)	0	
Maternal BMI at delivery (kg/m^2)	31.6 (28.6–37.1)	30.4 (26.6–34.6)	0.004
Low transverse cesarean	175 (92.1%)	247 (98.8%)	<0.001
Maternal medical problem[a]	68 (35.8%)	43 (17.2%)	<0.001
Number of prior cesareans	3 (3–3)	3 (3–4)	<0.001
Gestational age at delivery (weeks)	39 (37.9–39.1)	37.3 (36.7–38)	<0.001
Birthweight (kg)	3.3 (3–3.6)	3 (2.8–3.4)	<0.001

Abbreviation: BMI, body mass index.
Note: Data are presented as median (interquartile range) or *n* (%).
[a]Includes gestational and pregestational diabetes, chronic hypertension, thyroid dysfunction, cardiovascular disease, epilepsy, hemoglobinopathy, kidney disease, prior or active thrombosis, thrombocytopenia, asthma, inflammatory bowel disease, and systemic lupus erythematosus.

(3.7 vs. 0.4%; *p* = 0.042), as was maternal ICU admission (3.2 vs. 0.4%; *p* = 0.046). While the frequency of postpartum hemorrhage (defined as EBL > 1,000 mL) was more common in women who delivered at the hospital with a policy of delivery at 37 weeks (30.4 vs. 15.3%; *p* < 0.01), the frequency of blood transfusion was not different between cohorts (1.6 vs. 5.3%; *p* = 0.051). Finally, the composite maternal morbidity was more frequent in the 39-week delivery policy cohort compared with the 37-week delivery policy cohort (7.9 vs. 1.6%; *p* = 0.002).

Table 2 Bivariable analysis of maternal and neonatal complications stratified by delivery timing policy

	Policy of delivery at 39 wk	Policy of delivery at 37 wk	*p*-Value
Maternal outcomes			
Unscheduled surgery	78 (41.1%)	38 (15.3%)	<0.001
Maternal death	0	0	–
Cystotomy	7 (3.7%)	1 (0.4%)	0.024
Bowel injury	1 (0.5%)	1 (0.4%)	1.000
Maternal ICU admission	6 (3.2%)	1 (0.4%)	0.046
Hysterectomy	2 (1.1%)	2 (0.8%)	1.000
Postpartum hemorrhage	29 (15.3%)	75 (30.4%)	<0.001
Transfusion	10 (5.3%)	4 (1.6%)	0.051
Length of surgery (minutes)	60 (45–81)	64 (54–76)	0.078
Composite maternal morbidity[a]	15 (7.9%)	4 (1.6%)	0.002
Neonatal outcomes			
Neonatal death	0	0	–
5-min Apgar < 7	12 (6.4%)	1 (0.4%)	<0.001
NICU admission	23 (12.1%)	32 (12.9%)	0.803
NICU length of stay (days)	4 (2–16)	8 (4–19)	0.094

Abbreviations: ICU, intensive care unit; NICU, neonatal intensive care unit.
[a]Defined as present if cystotomy, bowel injury, hysterectomy, need for a blood transfusion, or maternal ICU admission occurred.

Bivariable analyses of neonatal outcomes are also given in ►**Table 2**. There were no neonatal deaths at either site. Compared with women who delivered at the hospital with a policy of delivery at 37 weeks, women who delivered at the hospital with a policy of delivery at 39 weeks were more likely to have an infant whose 5-minute Apgar score was less than 7 (6.4 vs. 0.40%; $p < 0.01$). There were no differences in NICU admission or NICU length of stay if admission occurred between the cohorts.

After adjusting for potential confounders, there were no differences in maternal cystotomy, ICU admission, or the composite maternal morbidity between cohorts (►**Table 3**). While postpartum hemorrhage remained significantly higher in the site with a policy of delivery at 37 weeks (adjusted odds ratio [aOR]: 3.25; 95% confidence interval [CI]: 1.63–6.46), there was no difference in transfusion between the cohorts (aOR: 0.27; 95% CI: 0.06–1.14). In terms of neonatal outcomes, there were no differences in the incidence of a 5-minute Apgar less than 7 between the cohorts.

Comment

There is no clear consensus on appropriate timing of delivery for women who have undergone three or more prior cesareans. While an uncomplicated pregnancy requiring a scheduled delivery typically occurs at 39 weeks' gestation or beyond, women with higher order repeat cesareans may, similar to women with prior classical cesareans or extensive uterine surgery, be at an increased risk of complications related to an unscheduled presentation and delivery. Whether scheduling an early term delivery would reduce these morbidities is unknown.

Table 3 Multivariable analyses of maternal and neonatal complications

	aOR[a] for policy of delivery at 37 wk compared with 39 wk	95% CI
Maternal complications		
Unscheduled cesarean	0.43	0.24–0.77
Cystotomy	0.15	0.01–1.65
Maternal ICU admission	0.18	0.02–1.84
Postpartum hemorrhage	3.25	1.63–6.46
Transfusion	0.27	0.06–1.14
Composite maternal morbidity	0.30	0.08–1.17
Neonatal complications		
5-min Apgar < 7	0.13	0.01–1.30

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; ICU, intensive care unit.
[a]Adjusting for age, race/ethnicity, body mass index, and any major maternal medical problems.

In this study, we found that a policy to deliver women with higher order cesareans in the early term period was associated a reduction in the need for unscheduled delivery. In addition, we observed an increased risk of postpartum hemorrhage compared with a planned 39-week delivery. There are some data that cesarean delivery performed at earlier gestational ages have an associated increased risk of postpartum hemorrhage.[19–22] Most of these morbidities arise from a less developed lower uterine segment in preterm uteri, often necessitating a classical uterine incision. However, our data demonstrated a higher incidence of nonlow transverse uterine incisions associated with a planned 39-week delivery; therefore, it is unlikely that uterine incision contributed to this observed difference. It is more likely that this observed association is because of other unmeasured clinical differences between the two sites. Estimations of blood loss at delivery are subjective; hospital-specific differences in ascertainment of this estimate likely influenced this finding, particularly given the absence of any significant difference in transfusion.

There were no differences in neonatal outcomes between the cohorts. While an early term delivery is associated with increased neonatal morbidity compared with delivery at 39 weeks,[16] the limited sample size may preclude the ability to detect potential differences in these morbidities. On the other hand, one might have expected the frequency of unscheduled cesareans to potentially result in neonatal morbidity. However, the site with a policy of planned 39-week deliveries has four obstetric operating rounds, dedicated 24/7 obstetric anesthesiology services, and an in-house obstetrician present for all obstetric emergencies. Future research should examine neonatal outcomes in more diverse resource settings.

One of the most feared sequelae of a previous cesarean is antepartum or intrapartum scar dehiscence and subsequent fetal compromise (asphyxia, neurologic damage, death).[19–22] In the case of uterine rupture, expedient delivery is essential for neonatal and maternal well-being. Many, though not all, studies have demonstrated an increased rate of uterine rupture in the case of multiple prior cesarean deliveries compared with one or two prior cesareans, and significant maternal and neonatal compromise is common in the case of uterine rupture.[21,23] Delivery in the early term period is meant to address some of the morbidities associated with antepartum scar dehiscence as well as any operative morbidity resulting from unscheduled delivery. Our study demonstrated that serious morbidities (maternal ICU admission, death) as well as operative complications (bowel injury, bladder injury) was not increased in the group delivered at 39 weeks; however, our sample size was too small to detect potentially clinically meaningful differences in these rare outcomes.

One of the strengths of our study is the relatively large number of subjects undergoing higher order cesareans divided between two centers with different policies of timing of such deliveries. However, despite the relatively large sample size, the rareness of the most serious sequelae—maternal death, hysterectomy, and neonatal death—preclude a definitive assessment of the relative safety of each

delivery policy. For example, given the observed incidences in maternal morbidities seen in the cohort with a policy of 37-week delivery, we had sufficient (80%) power to detect a minimum of a 10-fold increased incidence of bowel injury and a 5-fold increased incidence of transfusion. Smaller, but clinically significant, differences would not be identified with these data. Furthermore, the planned regression analyses may have been biased toward the null hypothesis, due to the small number of outcomes, and potential overfitting, due to the limited sample size. Moreover, by incorporating patients from two separate institutions, other potential hospital- or provider-level factors could confound any observed association, and definitive conclusions cannot be drawn from these data.

Given the possibility that early term delivery may reduce unscheduled deliveries without an increase in adverse neonatal outcomes, an adequately powered randomized trial should be undertaken to clarify the exact maternal and neonatal risks and benefits to early term delivery in women undergoing a high-order cesarean delivery.

Conflict of Interest
None.

References

1 Hamilton BE, Martin JA, Osterman MJK, et al. Births: final data for 2014. In: National Vital Statistics Reports. Hyattsville, MD: National Center for Health Statistics; 2014:1–64
2 MacDorman MF, Menacker F, Declercq E. Cesarean birth in the United States: epidemiology, trends, and outcomes. Clin Perinatol 2008;35(02):293–307
3 Gilliam M, Rosenberg D, Davis F. The likelihood of placenta previa with greater number of cesarean deliveries and higher parity. Obstet Gynecol 2002;99(06):976–980
4 Juntunen K, Mäkäräinen L, Kirkinen P. Outcome after a high number (4-10) of repeated caesarean sections. BJOG 2004;111(06):561–563
5 Clark EA, Silver RM. Long-term maternal morbidity associated with repeat cesarean delivery. Am J Obstet Gynecol 2011;205(6, Suppl):S2–S10
6 Lyell DJ. Adhesions and perioperative complications of repeat cesarean delivery. Am J Obstet Gynecol 2011;205(6, Suppl):S11–S18
7 Silver RM. Delivery after previous cesarean: long-term maternal outcomes. Semin Perinatol 2010;34(04):258–266
8 Zia S, Rafique M. Intra-operative complications increase with successive number of cesarean sections: myth or fact? Obstet Gynecol Sci 2014;57(03):187–192
9 Morales KJ, Gordon MC, Bates GW Jr. Postcesarean delivery adhesions associated with delayed delivery of infant. Am J Obstet Gynecol 2007;196(05):461.e1–461.e6
10 Tulandi T, Agdi M, Zarei A, Miner L, Sikirica V. Adhesion development and morbidity after repeat cesarean delivery. Am J Obstet Gynecol 2009;201(01):56.e1–56.e6
11 Rashid M, Rashid RS. Higher order repeat caesarean sections: how safe are five or more? BJOG 2004;111(10):1090–1094
12 Rahman MS, Gasem T, Al Suleiman SA, Al Jama FE, Burshaid S, Rahman J. Bladder injuries during cesarean section in a University Hospital: a 25-year review. Arch Gynecol Obstet 2009;279(03):349–352
13 Rossouw JN, Hall D, Harvey J. Time between skin incision and delivery during cesarean. Int J Gynaecol Obstet 2013;121(01):82–85
14 Spain JE, Tuuli M, Stout MJ, et al. Time from uterine incision to delivery and hypoxic neonatal outcomes. Am J Perinatol 2015;32(05):497–502
15 Maayan-Metzger A, Schushan-Eisen I, Todris L, Etchin A, Kuint J. The effect of time intervals on neonatal outcome in elective cesarean delivery at term under regional anesthesia. Int J Gynaecol Obstet 2010;111(03):224–228
16 Spong CY, Mercer BM, D'alton M, Kilpatrick S, Blackwell S, Saade G. Timing of indicated late-preterm and early-term birth. Obstet Gynecol 2011;118(2 Pt 1):323–333
17 Committee on Obstetric Practice, the American Institute of Ultrasound in Medicine, and the Society for Maternal-Fetal Medicine. Committee Opinion No 700: methods for estimating the due date. Obstet Gynecol 2017;129(05):e150–e154
18 Mourad M, Gupta S, Rebarber A, Saltzman DH, Fox NS. Effect of resident participation on outcomes in high-order cesarean deliveries. Obstet Gynecol 2015;126(Suppl 4):21S–26S
19 Bujold E, Gauthier RJ, Hamilton E. Maternal and perinatal outcomes associated with a trial of labor after prior cesarean delivery. J Midwifery Womens Health 2005;50(05):363–364
20 Guise JM, Denman MA, Emeis C, et al. Vaginal birth after cesarean: new insights on maternal and neonatal outcomes. Obstet Gynecol 2010;115(06):1267–1278
21 Landon MB. Predicting uterine rupture in women undergoing trial of labor after prior cesarean delivery. Semin Perinatol 2010;34(04):267–271
22 Lydon-Rochelle M, Holt VL, Easterling TR, Martin DP. Risk of uterine rupture during labor among women with a prior cesarean delivery. N Engl J Med 2001;345(01):3–8
23 Smith GC, Pell JP, Cameron AD, Dobbie R. Risk of perinatal death associated with labor after previous cesarean delivery in uncomplicated term pregnancies. JAMA 2002;287(20):2684–2690