Unfavorable impact of scheduled cesarean section at 36 gestational weeks for placenta previa

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Abstract

Background Pregnant women with no risk factors should have received elective CS later than 37 weeks because the incidence of respiratory disorder of neonates decreases [5-8]. Hence, the appropriate timing that CS for placenta previa was performed on the side of both the mother and neonate was unclear. This study aimed to evaluate the most appropriate timing of cesarean section (CS) in placenta previa cases.

Methods Singleton pregnant women who were scheduled to undergo an elective CS at 36 weeks (Group A) or 37 weeks of gestation (Group B) for placenta previa between August 2003 and July 2018 at our hospital were identified. The timing of CS was decided based on the judgment of the doctor with consideration of the risk of bleeding or faculties adaptation. Maternal and neonatal outcomes between both groups were retrospectively examined.

Results There were a total of 272 cases, with 76 cases assigned in Group A and 196 cases in Group B. There was no difference in emergency CS rate (p = 0.36), intraoperative hemorrhage (p= 0.86), total hemorrhage at delivery (p= 0.64), and additional treatment between Group A and Group B. The birth weight of neonates in Group A was smaller (p < 0.001) compared to those in Group B. Apgar scores of neonates at 1 minute (p = 0.04) and 5 minutes (p < 0.01) were lower in Group A than in Group B. Furthermore, neonatal hypoglycemia was higher in neonates of Group A (p < 0.02).

Conclusions Regardless of selection bias, there were no merits to perform CS for placenta previa at 36 gestational weeks on both mother and neonate sides. Further studies are required to evaluate when elective CS for placental previa should be scheduled.

Background
Placenta previa is a condition where the placenta lies low in the uterus and partially or completely covers the internal os [1]. When women with placenta previa try vaginal delivery, they develop massive hemorrhage because of the dilation of the internal os with tearing of placental attachments and the inability of the lower uterine segment myometrium to constrict the torn vessels [2,3]. Therefore, cesarean section (CS) was recommended as a method of delivery in women with placenta previa [4]. Recently, several studies have shown that pregnant women without any risk factors should have received elective CS later than 37 weeks because the risk of intraoperative hemorrhage associated with CS for mothers does not increase but the incidence of respiratory disorder of neonates decreases [5–8]. Hence, the most important factor about CS for mothers with placenta previa is the high incidence of intraoperative or postoperative massive hemorrhage because it could result into unfavorable obstetrical outcome such as the death of not only the mother but also the neonate [9–11]. As the gestational ages increase, the incidence of massive hemorrhage at CS for placenta previa increases gradually [12,13]. Particularly, the risk of major hemorrhage increases rapidly after 36 weeks of gestation [14]. Thus, Green-top Guideline of the Royal College of Obstetricians and Gynaecologists and the American College of Obstetricians and Gynecologists and the Guideline for Obstetrical Practice in Japan recommended CS for placenta previa from the first of 36 weeks until the end of 37 weeks of gestation [15–17]. However, there were less reports about the appropriate timing for CS for placenta previa [18], and it was unclear when CS for placenta previa was performed on the side of both the mother and neonate.

Herein, our study aimed to compare singleton women with placenta previa who were scheduled to undergo an elective CS at 36 weeks or 37 weeks of gestation and examine the appropriate timing of CS in placenta previa cases.
Methods

Singleton women with placenta previa who were scheduled to undergo an elective CS at 36 weeks or 37 weeks of gestation between August 2003 and July 2018 at our hospital were identified. Mothers who were scheduled to receive elective CS at 36 weeks of gestation or at 37 weeks of gestation were assigned as Group A and Group B, respectively. The timing of CS was decided based on the judgment of the doctors with consideration of the risk of bleeding, the extent of threatened premature labor, or the faculties adaptation. Maternal and neonatal adverse events of both groups were obtained from the medical records.

At our hospital, the basic management for placenta previa were as the previous report [19]. As a summary, placenta previa was diagnosed using transvaginal sonography and magnetic resonance imaging until 32 weeks of gestation. At the time of this diagnosis, the timing of CS was scheduled. However, when persistent antenatal bleeding defined as painless genital bleeding from the placenta with over 100 mL of blood loss or uncontrollable uterine contractions occurred, an emergency CS was performed. If the blood loss was increased during surgery or postoperatively, hemostatic procedures (e.g., gauze tamponade, brace sutures) were performed at the surgeon’s discretion between 2003 and 2014. Between 2015 and 2018, routine rapid insertion of Bakri balloon tamponade was intraoperatively performed regardless of hemorrhage. Even if massive bleeding did not stop after performing these procedures, uterine artery embolization, total abdominal hysterectomy, or reinsertion of Bakri balloon was performed.

Placenta previa was classified into major previa and minor previa. If the placenta covered the internal os, it was defined as major previa. If the leading edge of the placenta was in the lower uterine segment but did not cover the cervical os, it was defined as minor previa [20]. We intravenously administered tocolytic agents such as ritodrine hydrochloride and
magnesium sulfate to women who were threatened to have premature labor or developed antenatal bleeding. The amount of intraoperative hemorrhage was measured from the time of the skin incision to the time of scar closure, based on suction count and towel weight including amniotic fluid. Intraoperative hemorrhage was defined as bleeding from the end of the CS until skin closure. Intraoperative hemorrhage > 1500 mL including the amniotic fluid during CS was defined as massive hemorrhage, and we evaluated the risk factors of massive hemorrhage.

Statistical analysis

Statistical analysis was performed using χ2 test, Fisher’s exact test, and Mann-Whitney U test to evaluate the differences in characteristics and outcomes of pregnant women. Univariate and multivariate analyses were performed using logistic regression. Statistical significance was defined as a p value < 0.05.

Results

There were a total of 272 cases during the study period, with 76 cases assigned in Group A and 196 cases in Group B. The maternal characteristics and operative information of the two groups are shown in Table 1. In Group A, more cases were complicated with major placenta previa (p<0.01) and antenatal bleeding (p<0.01), and they were treated with tocolytic agents (p<0.01). There were no statistical significances in other factors between the two groups. Regarding operative information, there were no statistical significances in the rate of emergency CS (p = 0.36), intraoperative hemorrhage (p = 0.86), and additional treatment for massive hemorrhage except for intrauterine balloon tamponade (p = 0.011). The neonatal outcome is shown in Table 2. In Group A, the birth weight of neonates was significantly smaller (2511 g vs. 2678 g, p < 0.001), and Apgar scores of neonates at 1 minute (p = 0.04) and 5 minutes (p<0.01) were lower in Group A than in Group B.
Furthermore, transient tachypnea of the neonate \( (p = 0.047) \) and neonatal hypoglycemia \( (p = 0.02) \) were higher in Group A than in Group B. There were no statistical differences in other factors.

Univariate and multivariate analyses for potential factors contributing to massive hemorrhage of intraoperative hemorrhage at delivery are shown in Table 3. Multivariate analyses revealed that noninsertion of intrauterine balloon (hazard ratio \([HR], 1.96; p = 0.046\)) was the risk factor of massive hemorrhage. Scheduled CS at 37 weeks of gestation \((HR, 0.94; p = 0.81)\) was not related to massive intraoperative hemorrhage.

**Discussion**

In this study, plan to undergo an elective CS at 36 weeks of gestation did not increase the risk of hemorrhage associated with CS for placenta previa on the side of the mother. Furthermore, risk such as tachypnea associated with preterm labor increased on the side of the neonate.

With intraoperative hemorrhage being the risk factor during CS for placenta previa, several factors such as complete placenta previa, anterior placentation, and placenta adhesion were reported \([21–23]\). Moreover, previous reports have indicated that the incidence of massive hemorrhage at CS for placenta previa increased as the gestational ages advanced \([12, 13]\). In our study, fewer cases with major placenta previa were included in the group scheduled to undergo an elective CS at 37 weeks of gestation. As a result, there were no significant differences in intraoperative hemorrhage at delivery between women who were scheduled to undergo an elective CS for placenta previa at 36 weeks of gestation and 37 weeks of gestation. Therefore, we performed univariate and multivariate analysis for intraoperative hemorrhage to confirm whether schedule at 37 weeks of gestation was the risk factor of intraoperative hemorrhage. Consequently, only intrauterine balloon tamponade was associated with intraoperative hemorrhage. Our
previous reports demonstrated that rapid routine insertion of Bakri balloon could effectively reduce hemorrhage at delivery [19]. Thus, the use of Bakri balloon could delay the scheduled day CS for placenta previa without increasing intraoperative massive hemorrhage.

In pregnant women with placenta previa who underwent emergency CS, abrupt and massive hemorrhage occurred [24]. Because massive hemorrhage could result to serious complications, emergency CS should be avoided as much as possible for women with placenta previa. Hence, this is the same for the neonates. This setting could result to neonatal anemia, prematurity, and mortality [11,25,26]. In our study, there were no statistical significances of rate of emergency CS for both groups. Therefore, CS scheduled at 37 weeks of gestation was permissible.

According to the previous reports of the neonatal outcome following elective CS with low risk, even though the timing of delivery is at term, the incidence of adverse events including respiratory and other adverse neonatal outcomes gradually increased until 39 weeks of gestation [27]. Our study demonstrated that CS scheduled at 36 weeks of gestation increased neonatal adverse events such as respiratory disorder and neonatal hypoglycemia. Thus, CS scheduled at 37 weeks of gestation might be recommended on the side of the neonate. With these results, we assumed CS scheduled after 38 weeks of gestation for placenta previa might decrease neonatal adverse events such as respiratory disorder and neonatal hypoglycemia. However, it was a challenging problem. It was unclear whether CS scheduled after 38 weeks of gestation because of placenta previa did not increase the risk including massive hemorrhage or emergency CS on the side of the mother. Further study should examine this problem.

This study had several limitations such as the fact that this is retrospective study that was conducted in a single institution with a small sample size. Furthermore, there was a
selection bias that patients with high risk of massive hemorrhage were likely to be scheduled to undergo an elective CS at 36 weeks of gestation based on the judgment of the doctors. However, Blackwell SC et al. pointed out that there were available data to resolve the problem [18]. Therefore, we believed our results were useful for further studies.

In conclusion, there was no difference in maternal outcome between women who were scheduled to undergo an elective CS at 36 weeks or 37 weeks of gestation for placenta previa regardless of selection bias. On the other hand, neonatal complications increased in neonates of women who were scheduled to undergo an elective CS at 36 weeks of gestation. Based on this result, further studies are required to evaluate when elective CS for placental previa should be scheduled.

Abbreviation

CS: Cesarean section

Declarations

Disclosure of potential conflicts of interest

None.

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. For this type of study, formal consent is not required. For the retrospective analysis, informed consent was not obtained. This study was approved by the Clinical Research Ethics Committee of the National Defense Medical College (No 2998).

Consent to publication
All data was anonymised so individual consent for publication was not applicable.

Availability of data and materials

All data analysed in this study are available from the corresponding author upon reasonable request.

Competing interests

All authors declare that they have no competing interests.

Fundings

None.

Author Contribution

**Protocol/project development:** MO, MM, MT

Data collection or management: MO, MM, HI, SK, HM, TS, HK, TH, KT

Data analysis: MO, MM, HI, HS, MN

Manuscript writing/editing: MO, MM, MT

All authors have read and approved the manuscript.

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Tables

Table 1

Comparison of maternal characteristics in women who were scheduled to undergo an elective CS for placenta previa at 36 weeks of gestation (Group A) and 37 weeks of gestation (Group B)

| Variables                  | Group A (n=76) | Group B (n=196) |
|----------------------------|---------------|-----------------|
| Maternal history           |               |                 |
| Maternal age (y)           | 34.5 (21-42)  | 34 (18-44)      |
| Parity                     |               |                 |
| Primipara                  | 38 (50.0)     | 99 (50.5)       |
| Multipara                  | 38 (50.0)     | 97 (49.5)       |
| History of previous CS     |               |                 |
| Positive                   | 12 (15.8)     | 24 (12.2)       |
| Negative                   | 64 (84.2)     | 172 (87.8)      |
| Category                                      | Value              | Percentage  |
|----------------------------------------------|--------------------|-------------|
| **Placental classification**                 |                    |             |
| Major placenta previa                        | 50 (65.8)          | 82 (41.8)   |
| Minor placenta previa                        | 26 (34.2)          | 114 (58.2)  |
| **Placental position**                       |                    |             |
| Anterior uterine wall                        | 11 (14.5)          | 24 (12.2)   |
| Posterior uterine wall                       | 65 (85.5)          | 172 (87.8)  |
| **Tocolytic agent used**                     |                    |             |
| Positive                                     | 42 (55.3)          | 72 (36.7)   |
| Negative                                     | 34 (44.7)          | 124 (63.3)  |
| **Antenatal bleeding**                       |                    |             |
| Positive                                     | 33 (43.4)          | 40 (20.4)   |
| Negative                                     | 43 (56.6)          | 156 (79.6)  |
| **Operative information**                    |                    |             |
| Elective or emergency CS                     |                    |             |
| Elective CS                                  | 61 (80.3)          | 167 (85.2)  |
| Emergency CS                                 | 15 (19.7)          | 29 (14.8)   |
| Operative time (min)                         | 48 (19–221)        | 51 (17–189) |
| Intraoperative hemorrhage (mL)               | 1128 (410–4700)    | 1139 (265–6223) |
| **Additional treatment**                     |                    |             |
| Intrauterine balloon tamponade               |                    |             |
| Done                                         | 30 (39.5)          | 46 (23.5)   |
| Not done                                     | 46 (60.5)          | 150 (76.5)  |
| Total abdominal hysterectomy                 |                    |             |
| Done                                         | 2 (2.6)            | 0 (0)       |
| Not done                                     | 74 (97.4)          | 196 (100.0) |
| Uterine artery embolization                  |                    |             |
| Done                                         | 9 (11.8)           | 9 (4.6)     |
| Not done                                     | 67 (88.2)          | 187 (95.4)  |
| Allogeneic transfusion                       |                    |             |
| Done                                         | 12 (15.8)          | 17 (9.5)    |
| Not done                                     | 64 (84.2)          | 179 (90.5)  |
| Admission in the intensive care unit         |                    |             |
| Done                                         | 2 (2.6)            | 0 (0)       |
| Not done                                     | 74 (97.4)          | 196 (100.0) |
Abbreviations
CS, cesarean section

Table 2
Comparison of outcomes of neonates born from women who were scheduled to undergo an elective CS for placenta previa at 36 weeks of gestation (Group A) and 37 weeks of gestation (Group B)
| Variables                                | Group A (n=76) | Group B (n=196) |
|------------------------------------------|----------------|-----------------|
| Birth weight in grams                    | 2511 (1616–3165) | 2678 (2005–3820) |
| Gestational age at delivery              |                |                 |
| Before 36 weeks                          | 8 (10.5)       | -               |
| 36 weeks                                 | 68 (89.5)      | -               |
| Before 37 weeks                          | -               | 27 (13.8)       |
| 37 weeks                                 | -               | 169 (86.2)      |
| Apgar score at 1 minute                  | 8 (1–9)        | 8 (2–10)        |
| Apgar score at 5 minutes                 | 9 (4–10)       | 9 (6–10)        |
| Transient tachypnea of the neonate       |                |                 |
| Positive                                 | 20 (26.3)      | 31 (15.8)       |
| Negative                                 | 56 (73.7)      | 165 (84.2)      |
| Neonatal jaundice                        |                |                 |
| Positive                                 | 8 (10.5)       | 9 (4.6)         |
| Negative                                 | 68 (89.5)      | 187 (95.4)      |
| Neonatal hypoglycemia                    |                |                 |
| Positive                                 | 33 (43.4)      | 55 (28.1)       |
| Negative                                 | 43 (56.6)      | 141 (71.9)      |

Abbreviations: CS, cesarean section

Table 3
Univariate analyses and multivariate analyses for potential factors contributing to more than 1500 mL of intraoperative hemorrhage
| Variables                                      | Univariate analyses | Multivariate analyses |
|-----------------------------------------------|---------------------|-----------------------|
|                                               | Odds ratio (95% confidence interval) | p value | Odds ratio (95% confidence interval) |
|                                               |                      |          |                                      |
| Age                                           |                      |          |                                      |
| ≥ 34 years vs. 34 years                       | 1.04 (0.63–1.73)     | 0.87     |                                      |
| Parity                                        |                      |          |                                      |
| Primipara vs. multipara                       | 1.28 (0.77–2.12)     | 0.34     |                                      |
| Gestational age at delivery                   |                      |          |                                      |
| Scheduled 37 weeks of gestation vs.           | 0.94 (0.56–1.58)     | 0.81     |                                      |
| scheduled 36 weeks of gestation               |                      |          |                                      |
| History of previous CS                        |                      |          |                                      |
| Positive vs. negative                         | 0.87 (0.41–1.87)     | 0.73     |                                      |
| Tocolytic agent used                          |                      |          |                                      |
| Positive vs. negative                         | 1.07 (0.64–1.78)     | 0.80     |                                      |
| Antenatal bleeding                            |                      |          |                                      |
| Positive vs. negative                         | 1.07 (0.61–1.89)     | 0.81     |                                      |
| Mode of surgery                               |                      |          |                                      |
| Emergency vs. elective                        | 1.30 (0.66–2.56)     | 0.45     |                                      |
| Placental classification                      |                      |          |                                      |
| Major vs. minor                               | 1.43 (0.86–2.37)     | 0.17     |                                      |
| Placental position                            |                      |          |                                      |
| Anterior vs. posterior                        | 2.12 (1.03–4.35)     | 0.04     | 2.00 (0.97–4.13)                     |
| Intrauterine balloon tamponade                |                      |          |                                      |
| Not done vs. done                             | 1.96 (1.06–3.62)     | 0.03     | 1.88 (1.01–3.48)                     |

**Abbreviations**

CS, cesarean section