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Original Research

Changes in Cord Arterial Blood Gas Parameters by the Onset of Spontaneous Respiration during Delayed Cord Clamping

Ji Hye Koh[1], Hyo-Eun Kim[2], Suhyoon Choi[1], Jun-Woo Ahn[3,*]

[1]Department of Obstetrics and Gynecology, University of Ulsan College of Medicine, Asan Medical Center, 55055 Seoul, Republic of Korea
[2]Department of Obstetrics and Gynecology, Gyeonsang National University of Medicine, Gyeongsang National University Changwon Hospital, 51524 Changwon, Republic of Korea
[3]Department of Obstetrics and Gynecology, University of Ulsan College of Medicine, Ulsan University Hospital, 44033 Ulsan, Republic of Korea
*Correspondence: ahnjwoo@uuh.ulsan.kr (Jun-Woo Ahn)
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Abstract

Background: The initiation of crying is an easy way to evaluate neonatal condition. Doubt arises about a neonate's condition if the initiation of crying occurs late during delayed cord clamping (DCC). This study aimed to detect any difference in cord arterial blood gas (cABG) parameters depending on when spontaneous respiration (SR) started during DCC in a cesarean section. **Methods**: This retrospective study analyzed cABG results in relation to SR start time during DCC. The study included full-term (n = 41) and preterm (n = 17) neonates who were born by cesarean section with DCC. If the neonate cried within 60 s of DCC, the crying start time was considered as the time of the first SR. The cABG results of the preterm and full-term neonates were then examined. Each group was further divided into groups of 5, 10, and 30 s according to time-to-SR onset (time-to-SR). Subsequently, the cABG results were analyzed between these time-to-SR subgroups. The Mann–Whitney test was used for the comparisons, and $p < 0.05$ was considered statistically significant. **Results**: The time-to-SR was not significantly different in the preterm and full-term neonates. In preterm neonates, no significant difference was observed in any cABG parameter. In full-term neonates, the partial pressure of carbon dioxide ($PaCO_2$) was significantly higher in the time-to-SR (T) $\geq$5 s (T $\geq$5 s) subgroup than in the T $<$5 s subgroup ($p < 0.05$), and bicarbonate and $PaCO_2$ were both significantly higher in the T $\geq$10 s subgroup than in the T $<$10 s subgroup ($p < 0.05$). **Conclusions**: All neonates had normal cABG results regardless of the SR start time. However, given the small number of cases and limitations of this study, we cautiously suggest that maintaining DCC in cesarean deliveries may be considered, even when the start of crying is delayed. Especially, in preterm neonates with immature gas exchange mechanisms, the decision to maintain DCC must be carefully considered.

Keywords: DCC; spontaneous respiration; cesarean section; cABG

1. Introduction

Delayed umbilical cord clamping (DCC) allows the delivery of residual placental blood to a neonate. It is performed by clamping the umbilical cord more than 30 s after birth. Although performing DCC for more than 30 s is recommended, the exact definition regarding the duration remains unavailable [1]. According to a recent review article, DCC is beneficial to both preterm and full-term neonates [2]. Compared with early-cord-clamping, DCC reduces the need for anemia-induced blood transfusions and the incidence of intraventricular hemorrhage in preterm neonates [3]. In-hospital mortality is also decreased in preterm neonates with DCC experience [3–5]. Furthermore, DCC is associated with hematocrit increase and an improvement in iron stores in the first several months of life in full-term neonates [3]. The World Health Organization and international governing bodies for health care subsequently endorsed DCC [2]. However, in certain clinical situations, such as a nonvigorous neonate or a neonate requiring resuscitation, DCC is recommended to be avoided [6]. Similarly, early-cord-clamping is specifically advised in clinical situations such as maternal hemodynamic instability, maternal hemorrhage, abnormal placentation (placenta previa and abruption), and when the placental circulation is not assured, such as in cord avulsion or fetal growth restriction with abnormal Doppler sonography findings [6].

Clinically, when a neonate is nonvigorous immediately after birth (especially during a cesarean delivery), determining whether to proceed with DCC is difficult. In vaginal delivery, fetal status can be assessed by fetal heart rate monitoring (when available) until immediately before birth, but during a cesarean delivery, such an evaluation cannot be made until after birth. The Apgar score (omitting the heart rate) can be applied to assess neonatal condition on the cesarean operating table. Moreover, the initiation of crying, which represents well-established spontaneous respiration (SR) and a good transition from fetal to newborn life, is an another easy way to evaluate neonatal condition. If the initiation of crying is late during DCC, the neonate's condition might be unfavorable even when the placental circulation with its gas exchange is maintained.

This study aimed to investigate any difference in cord arterial blood gas (cABG) parameters, as well as neonatal outcomes, according to the start of SR during DCC in cesarean section.

2. Materials and Methods

2.1 Study Design and Patient Selection Criteria

The Department of Obstetrics and Gynecology at Ulsan University Hospital (Ulsan, Republic of Korea) began using 60 s DCC in March 2021, consistent with the most recent recommendation from the American College of Obstetricians and Gynecologists [6]. We retrospectively reviewed the records of mothers who had preterm or full-term deliveries via cesarean section with DCC at Ulsan University Hospital between March 2021 and February 2022. Preterm delivery was defined as a gestational age (GA) of less than 37 weeks at birth. DCC was omitted in deliveries with maternal hemorrhage, maternal hemodynamic instability, placental abruption, or fetal growth restriction with abnormal Doppler sonography findings. DCC was also avoided when the cesarean delivery was performed under general anesthesia, which is usually required in patients with any of the abovementioned conditions. We also excluded neonates with major anomalies (e.g., complex heart disease, lung lesions, fetal hydrops, and gastrointestinal conditions), which may affect neonatal condition immediately after birth. Maternal and neonatal information obtained from medical records included maternal age and GA, pregnancy complications (gestational diabetes mellitus, pregnancy-induced hypertension, fetal growth restriction, short-cervix preterm birth risk, preterm labor, or abnormal placentation), reason for preterm birth, neonate birthweight, Apgar scores at 1 and 5 min, and date of the last outpatient clinic visit. The Ulsan University Hospital Institutional Review Board approved our study protocol (file no.: 2021-10-031-002).

2.2 Procedure and Data Collection during DCC

In this study, DCC began when the fetus was released from the uterus (the time of birth). A nurse recording the birth time or an assistant participating in the operation then used the operating room electronic clock to measure the 60 s DCC. In neonates, SR should be observed through breathing, specifically by monitoring chest movements. However, in this study, we substituted this with the immediate detection of the first cry during cesarean section; this option can be more readily observed. If the neonate cried during that time, the crying start time was written in the surgical record and was considered as the time of the first SR. During DCC, the operator gently stimulated the neonate, maintained the body temperature, and performed gentle oral and nasal suction with a suction bulb (if necessary).

2.3 Statistical Analysis and Subgroup Comparisons

After cord clamping, umbilical artery blood was immediately obtained from the cord that remained connected to the placenta. Our institution adopted the single clamping procedure for cABG analysis, which included pH, bicarbonate (HCO_3^-), lactate, base excess of blood (BE_B) and extracellular fluid (BE_{ECF}), and partial pressures of oxygen (PaO_2) and carbon dioxide ($PaCO_2$). The cABG results of the preterm and full-term birth groups were then analyzed. Furthermore, each group was classified according to the time-to-SR onset (time-to-SR), particularly within times of 5, 10, and 30 s. The time-to-SR was determined by the researchers after reviewing the data. All of the statistical data were analyzed using the IBM SPSS Statistics software application (version 21.0; IBM Corporation, Armonk, NY, USA). Variables are presented as medians with ranges unless otherwise stated. Our data were not normally distributed; hence, the nonparametric Mann–Whitney U test was used instead of the parametric tests. Moreover, we did not adjust the analyses, and $p < 0.05$ was considered statistically significant.

3. Results

3.1 Pregnancy Characteristics

Table 1 presents the details of 54 pregnancies included in this study (preterm birth group: 15 pregnancies, with 17 neonates because of two twin gestations; full-term birth group: 39 pregnancies, with 41 neonates because of two twin gestations). Anomalies in the neonates did not affect their breathing. Genitourinary anomalies were the most common anomalies in the full-term birth group. Each obstetric complication that occurred in one pregnancy was counted separately. All preterm neonates have received at least one cycle of corticosteroid treatment, even if it is not a complete cycle.

In the preterm group, two had fetal distress requiring delivery, but DCC was still possible. One case involved premature rupture of the membrane associated with variable deceleration in the nonstress test. The other was oligohydramnios with fetal growth restriction but with normal Doppler sonography findings.

3.2 Neonate Characteristics

Table 2 details the characteristics of the 58 included neonates. The median GA at birth was 35.5 (32.2–36.6) weeks in preterm neonates and 38.1 (37.0–40.1) weeks in full-term neonates, with median birth weights of 2560 and 3070 g, respectively. Of the preterm birth neonates, nine were admitted to the neonatal intensive care unit (NICU), mainly because of prematurity; no intracranial hemorrhages were reported. Of the full-term birth neonates, two were admitted to the NICU (one because of continuous oxygen desaturation during feeding and the other because of a prenatal arachnoid cyst requiring examination). In the latter

Table 1. Pregnancy characteristics.

Variable	Preterm births	Full-term births
Pregnancies, n	15	39
Maternal age, years		
Median	33	35
Range	25–41	27–41
Singleton pregnancy, n	13	37
Twin pregnancy, n	2	2
Anomalies*, n	1 (cryptorchism)	11
Obstetric complications, n		
Pregnancy-induced hypertension	3	4
Gestational diabetes mellitus	1	3
Fetal growth restriction	6	8
Preterm labor risk	6	10
Oligohydramnios	4	5
Abnormal placentation		
Others		1 (thrombocytopenia)
Cesarean section indication, n		
Previous uterine surgery history	4	17
Obstetric complication	5	
Multiple pregnancy	2	2
Fetal distress	2	
Fetal position	1	4
Cesarean delivery maternal request		4
Cephalopelvic disproportion		4
Abnormal placentation		4
Pregnancy complication		2
Induction fail		1
Other	1	1
Changes in hemoglobin, g/dL	(n = 9)	(n = 34)
Median	1.5	1.8
Range	0.6–4.1	0.1–4.7

* Multiple anomalies in a single fetus were counted separately.

neonate, postnatal brain sonography revealed a 2.4 cm connatal cyst, which later developed into a grade I intracranial hemorrhage.

3.3 Time-to-SR

Time-to-SR was not significantly different in preterm and full-term neonates. In preterm neonates, the median time-to-SR was 3 s, with 30 s as the longest. In full-term neonates, the median time-to-SR was 2 s, with 45 s as the longest. Fig. 1 presents a scatterplot of time-to-SR against GA at birth, and no relationship was observed.

3.4 Comparing Time-to-SR Subgroups and cAGB Parameters

To compare the neonates in each of the preterm and full-term birth groups, we divided them according to the time-to-SR, such as time-to-SR of less than 5 s and 5 s or more (T $<$5 s and T $\geq$5 s subgroups, respectively). The cABG parameters were subsequently compared between the time-to-SR subgroups. In preterm neonates, none of the cABG parameters showed a significant difference. In full-term neonates, $PaCO_2$ was significantly higher in the T $\geq$5 s subgroup than in the T $<$5 s subgroup (Table 3). When the time-to-SR was classified into less than 10 s and 10 s or more (T $<$10 s and T $\geq$10 s subgroups, respectively), HCO_3^- and $PaCO_2$ were both significantly higher in the T $\geq$10 s subgroup than in the T $<$10 s subgroup of full-term neonates (Table 4). In addition, when the time-to-SR was divided using a 30-second threshold, HCO_3^- and BE_{ECF} were significantly higher in the T $>$30 s subgroup of full-term neonates. However, only two neonates belonged to this subgroup. In preterm neonates, the cABG parameters showed no statistically significant differences when using the 30-second threshold.

4. Discussion

This study aimed to detect any difference in cABG parameters depending on SR onset during DCC in cesarean section. Regardless of the SR start time and GA at birth, all of the cABG parameters were within the normal range. In

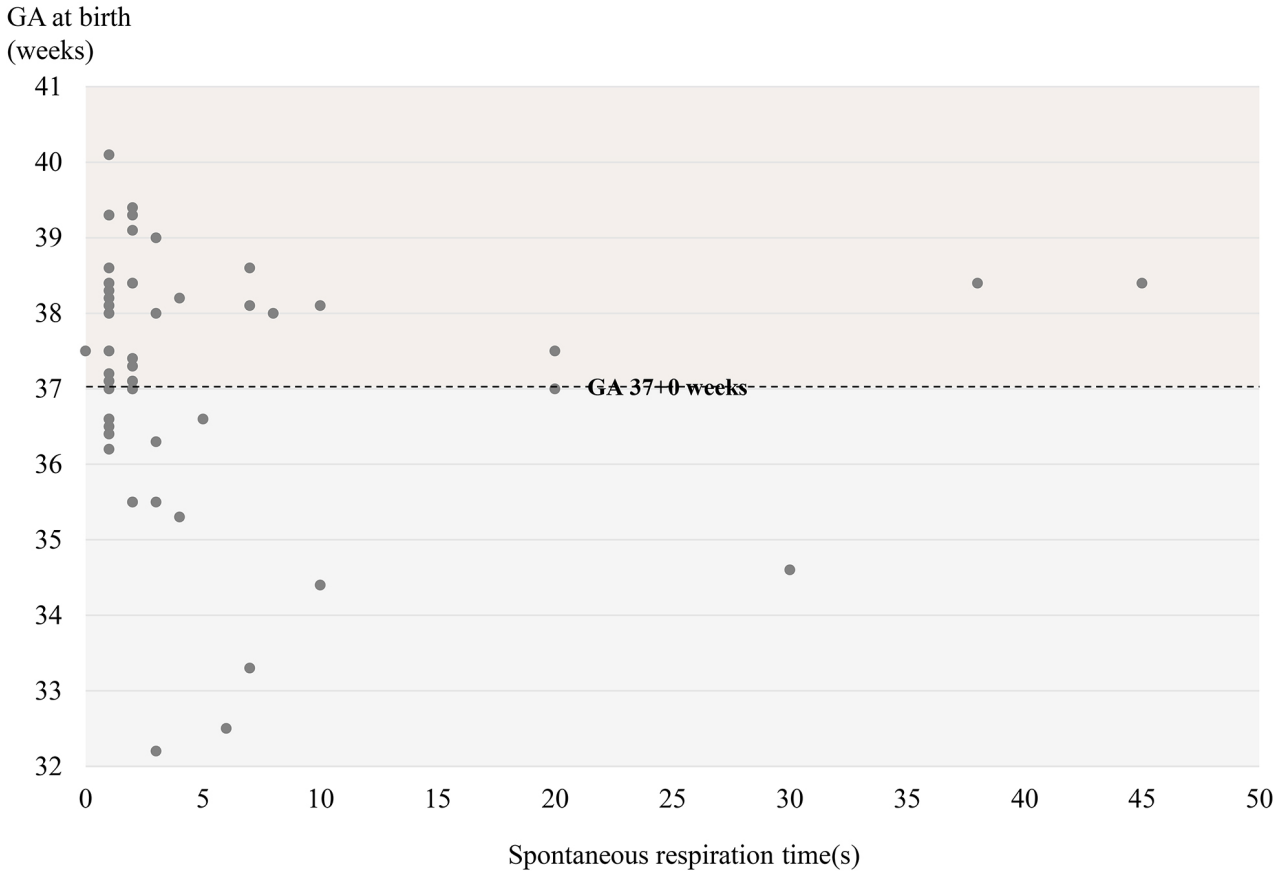

Fig. 1. Scatterplot of spontaneous respiration time. GA, gestational age.

Table 2. Neonate characteristics.

Variable	Preterm births	Full-term births
Neonates, n	17	41
Gestational age at birth and weeks		
Median	35.5	38.1
Range	32.2–36.6	37–40.1
Birth weight, g		
Median	2560	3070
Range	1510–2960	2070–4220
Apgar 1 min		
Median	8	9
Range	5–9	6–10
Apgar 5 min		
Median	9	10
Range	8–10	7–10
Time-to-SR onset, s		
Median	3	2
Range	1–30	0–45
Follow-up, days		
Median	63	30
Range	18–395	15–375
NICU admission, n	9	2
Intracerebral hemorrhage, n	0	1
Phototherapy, n	5	0

SR, spontaneous respiration; NICU, neonatal intensive care unit.

Table 3. Umbilical cord arterial blood gas analysis by the onset of spontaneous respiration before or after 5 s, mean values.

Variable	Time to spontaneous respiration					
	Preterm births (n = 17)			Full-term births (n = 41)		
	<5 s (n = 12)	≥5 s (n = 5)	*p* value	<5 s (n = 33)	≥5 s (n = 8)	*p* value
pH	7.34 ± 0.05	7.31 ± 0.05	0.195	7.34 ± 0.07	7.30 ± 0.07	0.186
HCO_3^-, mEq/L	25.59 ± 3.54	27.02 ± 2.48	0.383	24.82 ± 2.77	27.00 ± 2.90	0.073
Lactate, mmol/L	2.12 ± 0.36	2.14 ± 0.89	0.574	2.13 ± 1.06	2.39 ± 0.91	0.322
BE_B, mmol/L	−0.70 ± 2.79	−0.60 ± 2.11	0.959	−1.35 ± 2.02	−0.59 ± 3.01	0.198
BE_{ECF}, mmol/L	−0.12 ± 3.44	0.70 ± 2.43	0.574	−0.94 ± 2.40	0.63 ± 3.25	0.165
PaO_2, mmHg	16.13 ± 5.65	15.20 ± 9.12	0.879	40.73 ± 62.05	13.38 ± 8.21	0.084
$PaCO_2$, mmHg	47.62 ± 9.49	54.60 ± 8.88	0.195	46.48 ± 9.98	55.63 ± 9.44	0.032

HCO_3^-, bicarbonate; BE_B, base excess of blood; BE_{ECF}, base excess of extracellular fluid; PaO_2, partial pressure of oxygen; $PaCO_2$, partial pressure of carbon dioxide.

Table 4. Umbilical arterial blood gas analysis by the onset of spontaneous respiration before or after 10 s, mean values.

Variable	Time to spontaneous respiration					
	Preterm births (n = 17)			Full-term births (n = 41)		
	<10 s (n = 15)	≥10 s (n = 2)	*p* value	<10 s (n = 36)	≥10 s (n = 5)	*p* value
pH	7.33 ± 0.05	7.34 ± 0.08	1.000	7.34 ± 0.07	7.30 ± 0.06	0.301
HCO_3^-, mEq/L	25.77 ± 3.37	27.85 ± 1.77	0.235	24.84 ± 2.73	28.18 ± 2.55	0.024
Lactate, mmol/L	2.21 ± 0.50	1.45 ± 0.07	0.015	2.16 ± 1.06	2.34 ± 0.79	0.381
BE_B, mmol/L	−0.87 ± 2.64	0.85 ± 0.35	0.235	−1.44 ± 2.19	0.48 ± 1.84	0.076
BE_{ECF}, mmol/L	−0.13 ± 3.25	2.00 ± 0.57	0.235	−0.99 ± 2.49	1.90 ± 2.24	0.042
PaO_2, mmHg	14.77 ± 6.86	24.00 ± 1.41	0.088	38.67 ± 59.74	11.80 ± 10.31	0.108
$PaCO_2$, mmHg	49.23 ± 9.61	53.00 ± 12.73	0.618	46.92 ± 9.76	58.00 ± 10.91	0.042

HCO_3^-, bicarbonate; BE_B, base excess of blood; BE_{ECF}, base excess of extracellular fluid; PaO_2, partial pressure of oxygen; $PaCO_2$, partial pressure of carbon dioxide.

full-term neonates, $PaCO_2$ was significantly lower in those who cried earlier than in those who cried later; however, the pH was not significantly associated with the onset of SR. In preterm neonates, the cABG parameters were almost equivalent for any onset of SR. Thus, even if a preterm neonate cries late, the cABG parameters yield no effects that may potentially affect neonatal prognosis.

Studies on the relationship between SR and DCC and their associations with perinatal outcomes are limited, especially for cesarean delivery. Ersdal *et al.* [7] observed that the mortality rate in neonates tends to be higher if the cord is clamped before or immediately after the SR onset. In particular, 60% of their neonatal group with a poor outcome had a time interval between the first breath and cord clamping of less than 30 s. In our study, approximately 95% of our neonates started crying within 30 s of birth (occurring before DCC), and no fetal deaths occurred. In full-term neonates, only two were admitted to the NICU, including one for the postnatal work-up of a prenatal arachnoid cyst and the other for intermittent oxygen desaturation during feeding. Recently, several studies have been conducted on maintaining DCC while providing assisted ventilation as necessary during cesarean section for early preterm neonates. According to these studies, maintaining DCC while providing assisted ventilation to preterm neonates with inadequate breathing is feasible [8,9]. It confirmed umbilical vein pH values, but even with assisted ventilation, the values remained to have no significant difference. This finding is similar to our study, where even in preterm neonates who cried late, the pH values still did not significantly differ in the cABG analysis, although our study measured pH in the umbilical artery [8].

Studies on DCC and cABG have been conducted, but most of them included vaginal deliveries and different protocols. Longitudinal studies have measured changes in cABG parameters over time when DCC was performed. Conversely, some studies have compared cABG parameters between the DCC and early-cord-clamping groups. In a previous longitudinal study, pH decreased and PaO_2 increased over time when DCC was performed in vaginal deliveries [10,11]. Recently, Giovannini *et al.* [12] included cesarean deliveries and compared cABG parameters that were measured immediately after birth and 3 min later when DCC was performed in the cesarean and vaginal delivery groups. The cesarean deliveries had significantly increased pH and arterial lactate levels compared with vaginal deliveries, and the acid–base status tended to result in mixed acidosis. In our full-term cesarean deliveries, neonates with late SR onset tended to have lower pH and higher lactate, HCO_3^-, and $PaCO_2$ levels, although most of the differ-

ences were not statistically significant. One possible explanation is that a faster SR corresponds to a higher likelihood of compensation for mixed acidosis. However, our preterm cesarean deliveries also did not show such tendency. The prematurity of the neonate's gas exchange mechanism may have affected such results.

Most of the studies comparing cABG parameters between the DCC and early-cord-clamping groups have reported increased PaO_2 levels in the DCC group [13,14]. One previous study that included both cesarean and preterm deliveries reported that only PaO_2 was higher in the DCC group than in the early-cord-clamping group [13]. The authors of this study hypothesized that adjustment to cABG clinical reference intervals is not necessary for deliveries using DCC. Other studies have interpreted PaO_2 increment in DCC deliveries as a respiration effect of neonates [14]. Although the protocols and comparisons used in these previous studies were different from those in our study, our full-term neonates who started breathing earlier also tended to have increased PaO_2 levels. However, our preterm neonates who started breathing earlier did not demonstrate the same increased PaO_2 or decreased $PaCO_2$, possibly because of the prematurity of the neonate's gas exchange mechanism [15].

Our study's major advantage was the clinical assistance in performing DCC during cesarean deliveries. Cesarean delivery contributes to maternal hypotension because of spinal anesthesia and being in a supine position. Maternal hypotension may lead to placental hypoperfusion, transient fetal hypoxia, and subsequent metabolic acidosis [16,17]. Thus, determining whether DCC should be maintained for nonvigorous neonates, especially those who are not crying, is difficult. During cesarean section, SR, as represented by crying, is an easy way to assess neonatal condition. Nevertheless, cABG analysis is recommended to evaluate birth asphyxia and adverse perinatal events [1]. Currently, evidence on DCC efficacy in resuscitation scenarios reportedly remains limited. One small randomized study reported on safety outcomes for DCC in such scenarios. The preterm neonates who were included in the study had a median 1 min Apgar score of 2, which indicates weakness; however, those who underwent DCC demonstrated increased hematocrit level at 72 h and a decreased requirement for transfusions in the first 28 days of life [18]. Nonvigorous neonates are more likely to benefit from placental transfusion obtained through DCC because of the continued gas exchange occurring via the intact placental circulation [6]. In addition, the feasibility of applying resuscitation to prolong DCC for unstable neonates has been previously demonstrated [19,20]. More recently, the concept of physiology-based cord clamping (PBCC), which involves cord clamping when the neonate achieves stable SR with an adequate heart rate, was introduced and demonstrated to be beneficial [21]. Resuscitation can also be used to assist in achieving PBCC. However, the benefits of DCC and PBCC are not yet fully clear; thus, their application in nonvigorous neonates remains uncertain.

This study has several limitations that warrant discussion. First, the low number of neonates with late SR onset makes comparisons with early SR onset less reliable. Second, most of the preterm neonates were late preterm rather than early preterm; hence, this study may not adequately reflect information on early preterm neonates because late preterm neonates could be more similar to full-term neonates in some aspects. This similarity can be observed in our results. Third, this study equated SR with crying during the analysis. Some infants may begin SR without crying, whereas others may start crying without initiating SR. Differentiating these two actions during cesarean section is very challenging. Considering these limitations, to generalize the findings of this study, we need to evaluate as well the neonate's tone alongside crying when assessing the need for resuscitation. Additionally, conducting studies involving a higher number of neonates, particularly preterm ones, could provide more meaningful results using multivariate analysis and other statistical methods.

5. Conclusions

In all preterm and full-term neonates, all cABG parameters were within the normal range regardless of the SR start time. However, given the small number of cases and limitations of this study, we cautiously suggest that maintaining DCC in cesarean deliveries may be considered, even when the start of crying is delayed, while further research is needed to establish a more definitive recommendation.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

JHK designed the research study, wrote the manuscript. HEK and SC analyzed the data. JWA conceived the the study and gave final approval of the version to be published. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Ulsan University hospital Institutional Review Board (approval number: 2021-10-031-002).

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Conflict of Interest

The authors declare no conflict of interest.

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