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Delayed Cord Clamping In Very Preterm Infants Reduces The Incidence Of Intraventricular Hemorrhage And Late Onset Sepsis: A Randomized Controlled Trial

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Complete List of Authors:	Mercer, Judith S.; University of Rhode Island, Nursing, Midwifery; , Vohr, Betty R.; Brown Medical School, Pediatrics McGrath, Margaret; University of Rhode Island, Nursing Padbury, James F.; Brown Medical School, Pediatrics Wallach, Michael; Brown Medical School, Radiology Oh, William; Brown Medical School, Pediatrics
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3 Delayed Cord Clamping In Very Preterm Infants Reduces the Incidence of Intraventricular Hemorrhage
4 and Late Onset Sepsis: A Randomized Controlled Trial
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6 Judith S. Mercer, DNSc, CNM
7 University of Rhode Island, Kingston, RI
8

9 Betty R. Vohr, MD
10 Brown Medical School, Providence, RI
11

12 Margaret M. McGrath, DNSc
13 University of Rhode Island, Kingston, RI
14

15 James F. Padbury, MD
16 Brown Medical School, Providence, RI
17

18 Michael Wallach, MD
19 Brown Medical School, Providence, RI
20

21 William Oh, MD
22 Brown Medical School, Providence, RI
23

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25

26
27 Judith S. Mercer, DNSc
28 Professor, College of Nursing
29 University of Rhode Island,
30 2 Heathman Road,
31 Kingston, RI 02881
32 401-874-5303, Fax 401-874-2870
33 jmerc@uri.edu
34

35 Statistical Consultation: Jenifer Allsworth, Ph.D., Division of Research, Department of Obstetrics and
36 Gynecology, Women and Infants Hospital, Providence, Rhode Island and Yeong Kwak, R.N., Ph.D.,
37 University of Connecticut School of Nursing, Storrs, Connecticut.
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3 CONDENSATION
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6 The simple intervention of delayed cord clamping while lowering the infant appears to reduce the
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8 incidence of intraventricular hemorrhage and late onset sepsis in VLBW infants.
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12 Abbreviations
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14 BPD – bronchopulmonary dysplasia
15 CUS – cranial ultrasound
16 DCC – delayed cord clamping
17 ICC – immediate cord clamping
18 IVH – intraventricular hemorrhage
19 LOS – late onset sepsis
20 NEC – necrotizing enterocolitis
21 NICU – Neonatal Intensive Care Unit
22 PIH – pregnancy induced hypertension
23 ROP – retinopathy of prematurity
24 SNEC – suspected necrotizing enterocolitis
25 VLBW – very low birth weight
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3 ABSTRACT

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5 OBJECTIVE

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7 This study compared the effects of immediate (ICC) and delayed (DCC) cord clamping on VLBW infants
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9 on two primary variables: bronchopulmonary dysplasia (BPD) and suspected necrotizing enterocolitis
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11 (SNEC). Other outcome variables were late onset sepsis (LOS), and intraventricular hemorrhage (IVH).
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13 STUDY DESIGN

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15 This was a randomized controlled unmasked trial in which women in labor with singleton fetuses less than
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17 32 weeks gestation were randomized to ICC (cord clamped at 5 to 10 seconds) or DCC (30 to 45
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19 seconds). Women were excluded for the following reasons: their obstetrician refused to participate; major
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21 congenital anomalies; multiple gestations; intent to withhold care; severe maternal illnesses; placenta
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23 abruption or previa; or rapid delivery after admission.
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25 RESULTS

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27 Seventy-two mother/infant pairs were randomized. Infants in the ICC and DCC groups weighed 1151 (\pm
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29 379) and 1175 (\pm 346), and mean gestational ages were 28.2 (\pm 2.4) and 28.3 (\pm 2.1) weeks respectively.
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31 Analyses revealed no difference in maternal and infant demographic, clinical and safety variables. There
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33 were no differences in the incidence of our primary outcomes (BPD and suspected NEC). However,
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35 significant differences were found between the ICC and DCC groups in the rates of IVH (36% vs. 14%, p
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37 = 0.03) and LOS (22% vs. 3%, p = 0.03). Two (9%) of the 23 male infants in the DCC group had IVH
38
39 versus 8 (42%) of the 19 in the ICC group (OR 0.43, CI 0.24 to 0.76, p = .026). No cases of sepsis
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41 occurred in the 23 boys in the DCC group while six (32%) of the 19 boys in the ICC group had confirmed
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43 sepsis (p = .005). There was a trend towards higher initial hematocrit in the infants in the DCC group (49
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45 \pm 6 versus 46 \pm 6, p = .06).
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47 CONCLUSION

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49 Delayed cord clamping appears to protect VLBW infants from IVH and LOS especially for male infants.
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53 Key Words: delayed cord clamping, intraventricular hemorrhage, IVH, late onset sepsis, VLBW infants,
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55 randomized controlled trial
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INTRODUCTION

The current obstetrical practice in the United States is to clamp the umbilical cord of the very low birth weight (VLBW) infant immediately after delivery.¹ However, delaying cord clamping and lowering the infant below the perineum or incision site at cesarean section have been shown to significantly increase transfer of blood from the placenta to the infant.^{2,3} A delay of 30 to 45 seconds in cord clamping of preterm infants results in an 8 to 24% increase in blood volume (2 to 16 ml/kg after cesarean birth and a 10 to 28 ml/kg after vaginal birth).⁴ Immediate cord clamping may deprive the VLBW infant of essential blood volume and create a state of potential circulatory compromise⁵ resulting in hypotension,^{6,7,8} and poor perfusion of tissues.^{9,10}

Nine randomized controlled trials over the last decade have documented the safety and efficacy of delayed cord clamping in low birth weight or very low birth weight infants.¹¹ Benefits include higher blood pressure,^{7,12} higher hematocrit levels,¹³⁻¹⁵ more optimal oxygen transport and higher red blood cell flow,¹⁰ fewer days on oxygen and ventilation,¹⁶ fewer transfusions,^{14,16} and lower rates of IVH.^{17,18} Previous studies of cord clamping interventions, however, have been limited by small sample size, inconsistent definition of variables, and lack of follow-up beyond 6 weeks.¹¹

In a prior pilot study, we validated the feasibility and safety of the protocol for delayed cord clamping as well as immediate and short-term physiologic advantages of DCC.⁸ Findings included higher initial blood pressure, less suspected necrotizing enterocolitis, and fewer infants discharged on oxygen. Based on this pilot data, we hypothesized that the additional red blood cells obtained by delaying cord clamping may result in lower incidence of bronchopulmonary dysplasia (BPD).

The objective of this study was to compare the incidence of BPD in infants < 32 weeks gestation randomized to early (< 10 seconds) and late (30 to 45 seconds) cord clamping. The study was also designed to evaluate the effects of delayed cord clamping on other neonatal morbidities including suspected necrotizing enterocolitis (SNEC), late onset sepsis (LOS), intraventricular hemorrhage (IVH), and retinopathy of prematurity (ROP).

MATERIALS AND METHODS

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3 This randomized controlled trial was conducted between August 2003 and December 2004 at
4 Women and Infants' Hospital of Rhode Island (WIH). The study was approved by the Institutional Review
5 Boards at WIH and the University of Rhode Island. An independent data safety and monitoring committee
6 consisting of a maternal-fetal medicine obstetrician, a neonatologist, a nurse physiologist and a nurse
7 statistician reviewed the data after 14, and again, after 50 patients were randomized.
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11 The primary outcome variable was bronchopulmonary dysplasia (BPD) and the secondary
12 outcome variables were SNEC, IVH, LOS and ROP. Other outcome variables included: Apgar scores,
13 temperature on arrival in the NICU, the highest serum bilirubin level, initial and hourly blood pressures for
14 four hours, initial hematocrit, and need for blood transfusion during the infant's hospital stay.
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17 All women admitted between 24 and 31.6 weeks gestation with preterm labor were candidates for
18 inclusion in the study. The gestational age assessment using last menstrual period and/or early
19 pregnancy ultrasound was used to establish eligibility for the study. Exclusion criteria included:
20 obstetrician's refusal to participate, major congenital anomalies or multiple gestations, intent to withhold
21 care, severe maternal illnesses, or placenta abruption or previa. Women had to be admitted to the
22 hospital at least 2 hours before delivery to allow time for enrollment. Once a potential subject was
23 identified, approval of the attending obstetrician was obtained, the mother was approached, and written
24 informed consent was obtained.
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27 A statistician who was not involved in the trial developed a computer-generated random number
28 system. Block stratified randomization was used to assign the intervention to the subjects above and
29 below 28 weeks with a pre-specified equal probability to avoid unequal numbers of participants in each
30 gestational age group. Two sets of cards labeled for randomization were enclosed in sequenced, opaque
31 envelopes containing group assignment and kept in the Labor Unit. Research assistants who were
32 registered nurses and the PI (JSM) shared an on-call schedule to screen potentially eligible women,
33 enroll them, and attend the births. When called for a subject's impending birth, the PI or RN opened the
34 next randomization card, informed the staff of the group assignment, reviewed the protocol with the
35 attending obstetrician, attended the birth, and timed the cord clamping.
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38 Women were assigned to receive either immediate cord clamping (ICC) or delayed cord clamping
39 (DCC). For the ICC group, the obstetrician clamped the umbilical cord immediately (<10 seconds) after
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3 birth. For the DCC group, the obstetrician clamped the cord at 30 to 45 seconds and held the infant in a
4 sterile towel or blanket approximately 10-15 inches below the mother's introitus at vaginal delivery or
5 below the level of the incision at cesarean section. Care was taken that no tension or traction was placed
6 on the cord. A stopwatch was used to mark the time when the infant's buttocks were delivered from the
7 vagina or the uterus (or head if breech) and then the time elapsed was counted out in ten second
8 intervals for the obstetrician. At 30 to 45 seconds, the obstetrician clamped and cut the umbilical cord,
9 and the infant was moved to the radiant warmer for care. Infants in both groups were supplied with an
10 additional warming mattress (Transwarmer Infant Mattress, Cooper Surgical, Trumbull, CT) to assist in
11 maintaining temperature. The obstetricians could alter the protocol based on their clinical judgment
12 although this event did not occur throughout the course of the study. In the event that the timing of the
13 cord clamping was less than 30 seconds and the baby was randomized to the DCC group, a protocol
14 violation report was completed and the infant remained in the late clamped group (intention-to-treat).
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27 The subsequent clinical management of the infants was at the discretion of the attending
28 neonatologists. Because of the obvious nature of the intervention, the study could not be blinded. Our
29 institutional policy requires the presence of a pediatric staff member because of low gestation. However,
30 staff that attended each birth adhered to the PI's request not to reveal the infant's grouping in the infant's
31 medical records.
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37 Prenatal and delivery data were collected from the mothers' charts. Time of cord clamping,
38 placement of the infant, Apgar scores, and time and date of birth were collected in the Labor Unit. Infant
39 data were collected after 12 hours of age and after discharge. BPD was defined as requiring oxygen
40 therapy up to 36 weeks postmenstrual age or death. SNEC was defined as clinical impression when the
41 neonatology staff ordered an x-ray to rule out NEC and the infant was made NPO for at least 24 hours.
42 Cranial ultrasound (CUS) readings used the grading system of Papile: grade 1 is a germinal matrix
43 hemorrhage; grade 2 is extension into the lateral ventricle with blood filling less than 50% of the
44 ventricular area; Grade 3 is IVH with distension or dilatation of the lateral ventricles with blood; and
45 Grade 4 is IVH with parenchymal involvement. CUS were read by a single pediatric radiologist (MW) who
46 was blinded to the infant's grouping. Late onset sepsis was defined as blood culture positive in infants >
47 72 hours of age. Necrotizing enterocolitis was diagnosed based on Bell's criteria¹⁹ and retinopathy of
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3 prematurity was identified by an ophthalmologist per our routine eye examinations during the infants stay
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5 in the nursery.
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7 Power analysis was based on the event rate of bronchopulmonary dysplasia (56%) in the control
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9 group of our pilot study⁸ with a 30% relative reduction that would result in a 39% event rate. An alpha
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11 level of .05, and a beta level of .20 with a medium effect size ($r = .30$), was used to determine that 26
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13 babies were needed in each cord clamping interval group. An over sampling of 20% brought each group
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15 to 36 babies for a total of 72 subjects. All data were analyzed on an intention-to-treat basis. In spite of
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17 directional primary hypotheses, we used two-tailed tests to be as conservative as possible. Continuous
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19 variables were examined with Students t test and categorical variables were tested using Chi-square and
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21 Fisher's Exact test if cells contained counts less than 5. Logistic regression was used to control for
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23 gestational age and obtain odds ratios for significant findings.
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25 RESULTS

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27 Figure 1 shows the distribution of the 296 women who were admitted with preterm labor and who
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29 were screened for eligibility for this study. All further analyses were performed on the 72 randomized
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31 subjects.
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33 There were 7 protocol violations. Six occurred in the DCC group with cord clamping time ranging
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35 between 2 and 18 seconds instead of 30 seconds. These were mainly as a result of miscommunication
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37 at births. There was one protocol violation in the ICC group when a physician delayed clamping for 25
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39 seconds due to a misunderstanding of the protocol. All infants remained in their assigned groups for
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41 analyses.
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43 Table I shows no significance difference in maternal demographics, clinical characteristics and
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45 medical management.
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47 Table II shows no significant difference in the demographic and clinical characteristics of the
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49 study infants. Cord clamping time was significantly different per protocol—infants in the DCC group had
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51 significantly longer cord clamping times (32 seconds \pm 13 vs. 7 seconds \pm 4, $p < .001$). All other
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53 neonatal variables including those used for safety (1 and 5 minute Apgar scores, temperature on
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55 admission, serum bilirubin levels) were not significantly different between the groups.
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3 Table III shows that there were no significant differences in the incidence of death or BPD, NEC,
4 amount of blood loss and transfusion and ROP between the two groups. There were also no differences
5 between the infants in surfactant use (27 versus 24), days of ventilation (39 versus 35) , and oxygen use
6 at 28 days (11 versus 13) for the ICC and DCC groups respectively.
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11 Table IV shows that infants in the DCC group had less IVH (5 [14%] versus 13 [36%], $p = .03$)
12 during the first 28 days in the NICU. The incidence of IVH was equally divided between the stratified
13 groups (< 28 wks = 10; $28 \pm$ weeks = 8), although the majority occurred in infants less than 30 weeks
14 gestation (data not shown). In the infants less than 28 weeks, 7 (47%) of the 15 infants in the ICC group
15 had IVH versus 3 (21%) of the 14 infants in the DCC group (NS) while in those born after 28 weeks, 6
16 (29%) of 21 in the ICC group and 2 (10%) of 22 in the DCC group had IVH.
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23 Similar number of infants in each group received low dose Indomethacin for IVH prophylaxis
24 within the first 24 hours. All of the infants between 24 and 27 weeks had Indomethacin while 59 and 62%
25 received Indomethacin in the DCC and ICC groups respectively. The Grade 4 IVH was not seen until day
26 of life 12. One infant in the DCC group with IVH was a protocol violation and had immediate cord
27 clamping.
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33 We compared all infants with IVH ($n = 18$) with all infants without IVH ($n = 54$). Infants with IVH
34 had shorter time between birth and cord clamping (13 seconds versus 22 seconds, $p = 0.04$) and were
35 less likely to have had a cesarean delivery (3 [17%] vs. 15 [48%], $p = 0.03$). There was no relationship
36 between IVH and sepsis.
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40 Table IV shows that infants in the DCC group were less likely to have blood culture-proven sepsis
41 during the NICU stay (3% vs. 22%, $p = 0.03$). Six cases of confirmed sepsis occurred in the 24 to 27
42 week infants while 3 were in infants 28 to 31 weeks. Of the 9 infants who had late onset sepsis, 7 (78%)
43 occurred between 11 and 18 days of age. Infants with sepsis had lower initial hematocrit levels at birth
44 (48 ± 6 versus 42 ± 5 , $p = .03$) even when controlling for gestational age.
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50 Analyses by gender revealed that male infants had an advantage with DCC for IVH, sepsis, and
51 NEC. Gender effects are shown in Table 5.
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3 There were no adverse events or deaths in the DCC group. Three infants died in the ICC group.
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5 The causes of death included fulminating NEC (2) and terminal respiratory failure with probable sepsis
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7 syndrome.
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10 Further multivariate analyses were performed to evaluate the association of cord clamping with
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12 IVH and late onset sepsis. The impact of cord clamping group on IVH was evaluated adjusting for
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14 gestational age and cesarean section. The final model indicated that the IVH rate was more than 3 times
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16 higher in the ICC group (OR 3.5, 95% CI 1.1 – 11.1). A similar model for late onset sepsis adjusted for
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18 gestational age showed that infants in the DCC group were less likely to have sepsis (OR 0.10, 95% CI
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20 .01-.84).

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22 The eligible women not enrolled during the study period did not differ from the 72 randomized
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24 participants on any of the demographic variables. They differed from randomized women only in antenatal
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26 steroid use (87% vs. 100%, $p = 0.01$), PROM in hours (20 ± 36 versus 40 ± 45 , $p = 0.01$, and Cesarean
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28 section rate (64% versus 40%, $p = 0.01$). Infants of eligible women not enrolled differed from study infants
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30 only on admission temperature (96.3 ± 1.4 versus 97 ± 1.4 , $p = .01$). There was no significant difference
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32 in the overall incidence of IVH (25% versus 18%, $p = 0.35$) or sepsis (3% versus 8%, $p = 0.42$) between
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34 the subjects and the infants of eligible women not enrolled.

35 DISCUSSION

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37 Our primary null hypothesis was that infants in the DCC group would have the same rate of BPD
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39 based on the results from the pilot study. The null hypothesis proved to be true. The reason for the failure
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41 to reject the null hypothesis is that the study event rate of BPD in the ICC group (25%) turned out to be
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43 much lower than the event rate used for sample size calculation (56%) resulting in an underpowered
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45 estimate. The finding that DCC resulted in less IVH and less sepsis was unanticipated.

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47 Our data indicates that a brief delay in cord clamping time accompanied by lowering the infant to
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49 hasten the placental transfusion offers protection from IVH and late onset sepsis. The fact that the
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51 groups had almost identical demographic and baseline characteristics shows that the randomization
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53 process was successful. As in our previous pilot study, this study provided evidence that the protocol
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55 does not put even the smallest infants at risk of harm.⁸
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3 The theoretical foundation for the study was that the additional blood volume received as a result
4 of DCC would help to reduce neonatal morbidity by providing more blood volume and improving
5 cardiovascular stability. The preterm infant has less fetal-placental blood volume in his body at any point
6 in time than the term infant making him more likely to have a deficit if immediate clamping occurs.²⁰ The
7 high pressure in the placental circulation continues briefly after birth and fosters transfer of blood to the
8 infant.²¹

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15 The increase in cardiac output to the lung from 8% during fetal life to the 45% immediately after
16 birth necessitates transfer of an adequate blood volume.²⁰ When the cord is clamped before an adequate
17 placental transfusion to the infant has occurred, blood volume may be taken from other capillary beds
18 resulting in relative hypoperfusion.²² A potential circulatory effect of relative hypoperfusion may be
19 disruption of the autoregulation essential to stabilize cerebral blood flow and prevent a pressure-passive
20 circulation.²³ If the baby is not hemodynamically stable, there may be ischemic injury to the brain,²⁴ the GI
21 tract and the lung.

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29 Reduced blood volume does not necessarily result in immediately reduced blood pressure or
30 lower hematocrit as the infant's cardiovascular system increases vascular resistance to stabilize blood
31 pressure.²⁵ Increased capillary permeability in the preterm newborn allows rapid fluid shifts.⁵ These
32 factors, and lack of available accurate measurement techniques for blood volume, make hypovolemia
33 difficult to verify in the newborn, even though its effect may be profound. DCC allows time for placental
34 transfusion to supply essential blood volume to the infant and lowering the infant speeds the transfer of
35 blood volume.²⁶

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43 The finding that IVH was higher in the immediately clamped group is consistent with the recent
44 meta-analysis of RCTs on DCC in PT infants.¹¹ Other authors have reported reduced cerebral blood
45 volume preceding development of IVH.^{27, 28} Any reduction in IVH is important because of its association
46 with later morbidity, mortality and/or developmental delay.²⁹ Even Grades I and 2 are not without
47 sequelae.³⁰

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Our nursery practiced prophylactic Indomethacin to prevent IVH based on the study of Ment et
al.³¹ However, the number of infants receiving this intervention was similar between the two study groups.

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3 All the infants with confirmed late onset sepsis (LOS) had immediate cord clamping. The one
4 listed for the DCC Group was a protocol violation and her cord was clamped at 3 seconds. This finding is
5 important as LOS continues to be an important cause of morbidity and mortality in the NICU and
6 neurodevelopmental delay.³² We speculate that sepsis may be a result of immuno-compromise due to
7 loss of protective primitive hematopoietic progenitor cells along with blood volume at birth. The cord
8 blood of preterm infants (24-31 weeks) contains the highest concentration of primitive hematopoietic
9 progenitor cells and long-term culture-initiating cells when compared to the cord blood of infants closer to
10 term.³³
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19 The apparent protective effect of delayed cord clamping for the male infants suggests the
20 hypothesis that the additional blood volume the infant obtains may have gender-specific neuroprotective
21 and immunoprotective effects. This finding is of interest since there is increasing evidence of gender-
22 specific differences in neonates. For example, indomethacin, has been shown to exhibit gender-specific
23 effects on cerebrovascular reactivity, which were associated with a significantly decreased rate of IVH in
24 boys.³⁴
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31 Limitations of this study are that the primary null hypothesis was accepted because the study was
32 underpowered due to the use of a high event rate from our pilot study and the rejection of secondary null
33 hypothesis that is unanticipated. Nonetheless, the fact that our findings are consistent with the result of
34 the recent meta-analysis,¹¹ strengthens the idea that these findings are generalizable to the population of
35 very low birth weight preterm infants. This study adds to the growing body of knowledge on the benefits of
36 delayed cord clamping in preterm infants.¹¹ It may be that the small amounts of addition blood preterm
37 infants obtain by delaying cord clamping helps to stabilize cerebral blood flow, autoregulation, increase
38 oxygen delivery to vulnerable tissues, prevent ischemia, and cytokine release, and provide additional
39 stem cells to establish adequate immunocompetence.
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48 We have demonstrated that a brief delay in cord clamping time, accompanied by lowering the
49 infant to hasten the placental transfusion, offers protection from IVH and late onset sepsis. The innovation
50 of this study is the simplicity of the intervention of delaying cord clamping 30 to 45 seconds and lowering
51 the infant. The additional blood volume received appears to contribute to the improved outcomes of tiny
52 preterm infants.
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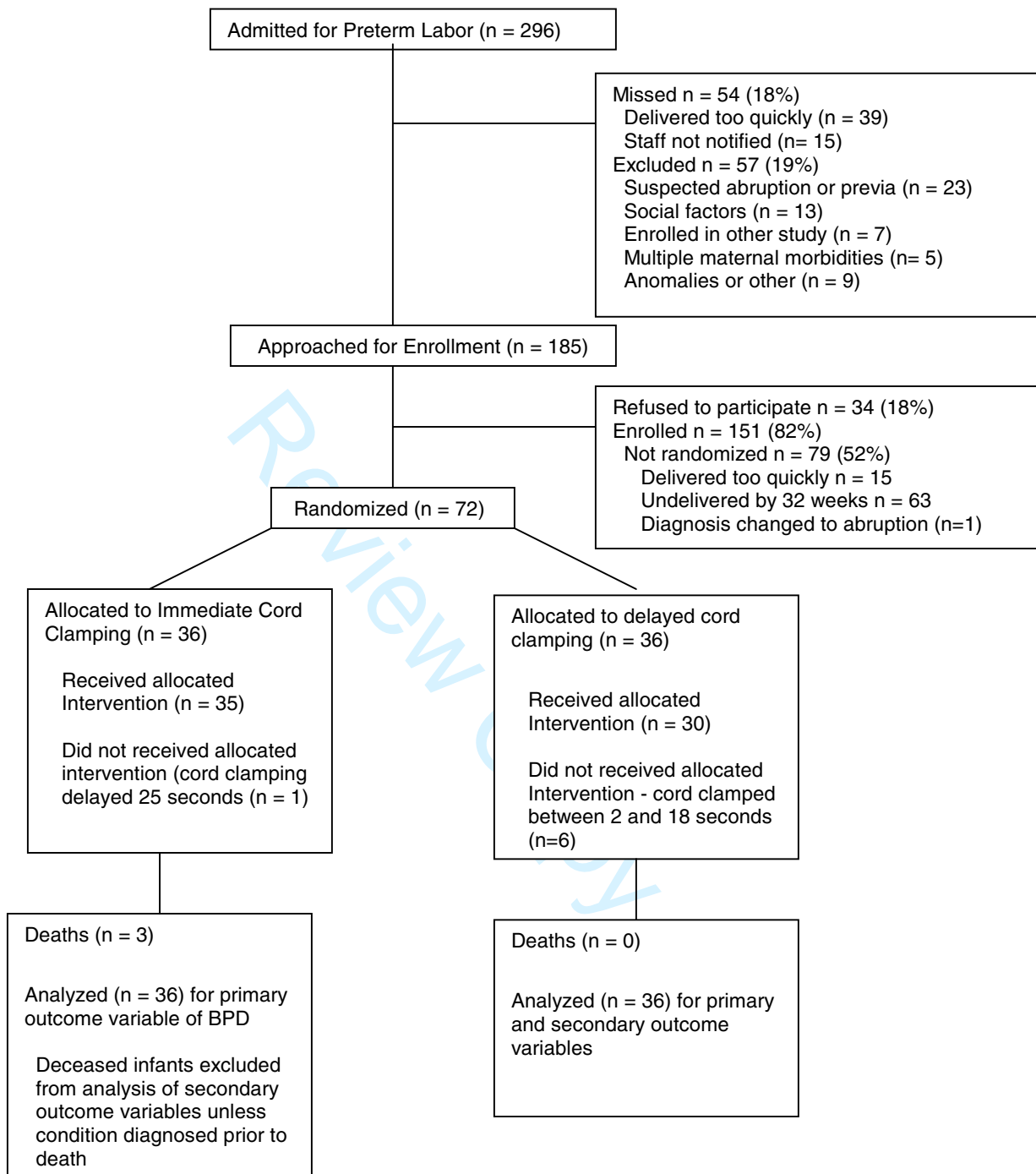
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Figure 1.



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3 Legend for Figure 1.
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7 Flow of women admitted for preterm labor between August 2003 and November 2004 including
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9 participants in Cord Clamping Study
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Table I.

Maternal Demographics, Clinical Characteristics, and Prenatal Medical Management

Characteristics	ICC (n =36)	DCC (n =36)
Mother's Age (yrs) mean + SD	26.8 ± 6.5*	27.1 ± 6.7
Primiparas	25 (69)	23 (64)
Race		
Black	4 (11)	5 (14)
White	20 (56)	18 (50)
Hispanic	11 (30)	11 (31)
Other	1 (3)	2 (6)
Public Insurance	17 (47)	15 (42)
Received Antenatal Steroids	36 (100)	36 (100)
Received Antenatal MgSO ₄ in 24 hrs before birth	21 (58)	14 (39)
PROM in hours	40 ± 44*	41 ± 47
Cesarean Section	14 (39)	15 (43)
Reasons for Preterm Birth**		
PROM	19 (53)	18 (50)
Preterm Labor	19 (53)	16 (44)
Presumed Chorioamnionitis	10 (28)	11 (31)
Incompetent Cervix	5 (14)	7 (19)
PIH	5 (14)	5 (14)

*Mean + SD. () = %. None of the differences are statistically significant.

**Some mothers had more than one condition.

Table II. Neonatal Demographic , Clinical and Safety Variables

	ICC (n =36)	DCC (n =36)	P Value
Birth weight, g*	1151 ± 379	1175 ± 346	n.s.
Gestational age (weeks)	28.2 ± 2.4	28.3 ± 2.1	n.s.
24 to 27 ⁶ weeks (No.)	15	14	
28 to 31 ⁶ weeks (No.)	21	22	
Male/Female ratio	19/17	23/13	n.s.
Apgar Score Median			
1 min	7 (1-9)	7 (1-9)	n.s.
5 min	8 (1-9)	8 (2-9)	
Temperature on admission to NICU, °Farenheit, (range)	96.8 ^o ± 1.5 ^o (92.8 ^o – 99.3 ^o)	97.1 ^o ± 1.2 ^o (94 ^o – 99.4 ^o)	n.s.
°Celcius, (range)	36 ^o ± 0.8 ^o (33.8 ^o – 37.4 ^o)	36.2 ^o ± 6 ^o (34.4 ^o – 37.4 ^o)	
Maximum serum Bilirubin (mg/dl) (Range)	9.5 ± 2.10 (5.5-13.8)	10.1 ± 2.4 (6.6-15.1)	n.s.
Initial Hematocrit (%)	46 ± 6 (34 – 60)	49 ± 6 (37 - 62)	.06
Mean of 1 st 4 hrs Mean Blood Pressure	31.9 ± 6	33.8 ± 4.5	n.s.
SNAP TM Scores	13.3 ± 12	12.3 ± 11	n.s.
Cord Clamp Time (sec)	6.9 ± 4.3 (1-25) (median = 5)	32.1 ± 12.6 (2-49) (median = 33)	<.001

*Mean ± SD, (range), n.s. = non significant

Table III. Neonatal Morbidities, Blood Loss and Transfusions

	ICC (n = 36)	DCC (n = 36)
	n (%)	n (%)
Death or BPD (O ₂ therapy @ 36 weeks)	9 (25)	8 (22)
*Discharge on O ₂	4 (12)	5 (14)
Suspected NEC	20 (56)	14 (39)
NEC, Bell ¹⁹ Stage		
No sign	25 (69)	27 (75)
1a	7	6
1b	0	2
2a	1	1
3b	2	0
Perforation	1	0
Blood Loss – Week 1, mL	11.4 ± 5.8	11.3 ± 5.7
# of Infants Transfused	22 (61)	18 (50)
# of Transfusions	2.47 ± 3.7	1.94 ± 3.1
Total Amount Transfused, mL	33 ± 45	27 ± 42
*ROP (all)	13 (40)	10 (28)
Deaths	3 (8)	0

*= n of 33 for ICC group as 3 infants in the ICC died before 1 month of age.

None of the differences are statistically significant.

Table IV. IVH and LOS in study infants

	ICC (n = 36)	DCC (n = 36)	p Value	Odds Ratio	95% CI
IVH					
All IVH	13 (36%)	5 (14%)	0.03	3.5	1.1 to 11
Grade 1	4 (11%)	3 (8%)			
Grade 2	8 (22%)	2 (6%)			
Grade 4	1 (3%)	0 (0%)			
Sepsis	8 (22%)	1 (3%)	0.03	.01	0.01 to 0.84

Table V. Gender differences in IVH, LOS, and NEC among infants with ICC and DCC.

	ICC		DCC	
	Boys (n = 19)	Girls (n = 17)	Boys (n = 23)	Girls (n = 13)
IVH	8 (42%)*	5 (29%)	2 (9%)	3 (23%)
Sepsis	6 (32%)*	2 (12%)	0	1 (8%)
NEC	3 (16%)*	1 (6%)	0	2 (15%)

*Differences for boys between groups, $p < .05$, Fisher's Exact Test.

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