POSITION STATEMENT

Umbilical cord management in preterm and term infants

Principal author(s)

Sarah D McDonald MD, Michael Narvey MD, William Ehman MD, Venu Jain MD PhD, Krista Cassell MD, The Society of Obstetricians and Gynecologists of Canada, Canadian Paediatric Society Fetus and Newborn Committee

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Abstract

Objectives: To assess the impact of deferred (delayed) cord clamping (DCC) and umbilical cord milking in singleton and twin gestations on maternal and infant mortality and morbidity.

Intended users: Maternity and newborn care providers.

Target population: Women who are pregnant with preterm or term singletons or twins.

Evidence: Searches of Medline, PubMed, Embase, and the Cochrane Library from inception to March 2020 were undertaken using Medical Subject Heading (MeSH) terms and key words related to deferred cord clamping and umbilical cord milking. This document represents an abstraction of the evidence rather than a methodological review.

Validation methods: This guideline has been reviewed by the Clinical Practice – Obstetrics Committee of the SOGC and approved by the SOGC Council and the Canadian Paediatric Society (CPS) Fetus and Newborn Committee.

Benefits, harms, and/or costs: In preterm singletons, DCC for (ideally) 60 to 120 seconds, but at least for 30 seconds, reduces infant risk of mortality and morbidity. DCC in preterm twins is associated with some benefits.

In term singletons, DCC for 60 seconds improves hematological parameters. In very preterm infants, umbilical cord milking (UCM) increases risk for intraventricular hemorrhage.

Terms and Abbreviations

'Preterm' is defined as ≤37 weeks, 'very preterm' as <32 weeks, and 'extremely preterm' as <28 weeks gestational age.

CI	confidence interval
DCC	deferred (delayed) cord clamping
GA	gestational age
ICC	immediate cord clamping
IVH	intraventricular hemorrhage
MD	mean difference
IUGR	intrauterine growth restriction
NEC	necrotizing enterocolitis
OR	odds ratio
RCT	randomized controlled trial
RR	relative risk
SGA	small for gestational age
TAPS	twin anemia polycythemia sequence
TTTS	twin-to-twin transfusion syndrome
UCM	umbilical cord milking

Recommendations

For ease of implementation, recommendations for preterm versus term infants have been kept distinct. Note that as the preterm period progresses, the risks of prematurity decrease substantially, such that the absolute benefits of DCC also decrease.

1. Singletons:
   a. *In both preterm (<37 weeks) and extremely preterm (<28 weeks) singletons*, deferred cord clamping (DCC) is recommended for 60 to 120 seconds because it decreases newborn mortality and morbidity and improves hematological outcomes after the newborn period. When cord clamping cannot be deferred for a full 60 to 120 seconds, then DCC for at least 30 seconds is superior to immediate clamping. DCC should be performed with the infant at or below the level of the introitus or at the level of the caesarean incision, as per Figure 1 (Strong, High).
   b. *In term singletons*, DCC is recommended for 60 seconds because it improves hematological outcomes at birth and past the newborn period. DCC beyond 60 seconds increases the risk of hyperbilirubinemia requiring phototherapy. DCC can be performed with the infant at or below the level of the introitus, or at the level of the caesarean incision (Strong, High), or on the mother's abdomen (Conditional, Low).
2. Stabilization or resuscitation with an intact cord for longer durations in preterm and term infants is feasible for centres with appropriate experience and equipment, although larger trials are needed to understand benefits and risks (Strong, Moderate).
3. For maintenance of temperature during DCC:
   a. *Preterm* infants should be placed in warm towels, medical grade plastic bags, or medical grade plastic wrap to maintain temperature (Strong, High).

   b. *Term* infants can be placed in warm towels or on the mother's abdomen (Conditional, Low).
4. Twins:
   a. In *preterm twins*, DCC is associated with some benefits and should be considered, except when contraindicated (Conditional, Low).
   b. In *term twins*, DCC may be considered based on presumed extrapolation of benefits in term singletons, except when contraindicated (Conditional, Low).
   c. The evidence regarding optimal duration of DCC in twins is insufficient. DCC for 30 to 60 seconds can be considered (Conditional, Low).
   d. When DCC is performed, *not* delaying delivery of the second twin is recommended (Conditional, Low).
5. Uterotonic medications increase uterine tone to prevent postpartum hemorrhage:
   a. *In preterm pregnancies*, due to concerns about a potential bolus of blood to preterm infants, it is recommended that intravenous (IV) uterotonic medications be administered after clamping the cord (Conditional, Low).
   b. *In term pregnancies*, with lower risk for bolus effects of blood, lower benefits of deferred cord clamping, and higher risk for maternal postpartum hemorrhage, it is recommended that IV uterotonic medications be administered with delivery of the anterior shoulder of the final infant (Conditional, Low).
6. Absolute contraindications to DCC are few, and include (but are not limited to) fetal hydrops, the need for immediate resuscitation of mother or infant (except in centres with appropriate experience and equipment), disrupted utero-placental circulation (e.g., bleeding vasa previas), and known twin-to-twin transfusion syndrome (TTTS) or twin anemia polycythemia sequence (TAPS). (Strong, High).
7. Relative contraindications to DCC are few but include (in term infants) risk factors for significant hyperbilirubinemia (e.g., significant polycythemia, severe intrauterine growth restriction (IUGR), pregestational diabetes), and cases where maternal antibody titres are high or when the first infant in a pair of monochorionic twins is delivered. In all these circumstances, immediate cord clamping should be considered (Conditional, Low).
8. Cautions regarding DCC are few but include (in preterm infants) risk factors for significant hyperbilirubinemia (e.g., significant polycythemia, severe IUGR, and cases where maternal antibody titres are high or when the first infant in a pair of monochorionic twins is delivered. In all these circumstances, discussion with the newborn's care providers regarding benefits and risks and the duration of DCC is encouraged. The infant's gestational age should be taken into account, with consideration of deferral for 30 seconds (Conditional, Low).
9. Umbilical cord milking (UCM):
   a. UCM is *not* recommended in very preterm infants <32 weeks, due to increased risk for severe intraventricular hemorrhage (IVH) (Strong, Moderate).
   b. In preterm and term infants, DCC should be performed instead of UCM (Strong, High).

The rationale for umbilical cord management

Best practices for umbilical cord management enhance the transfer of blood from placenta to newborn. Deferred cord clamping (DCC) involves waiting before clamping the cord, while umbilical cord milking (UCM) involves squeezing cord blood toward the infant one or more times [1]. The term 'deferred cord clamping' better expresses a choice of practice, and is used instead of 'delayed cord clamping' (which suggests being late to act) in this statement. DCC and UCM help to increase blood volume as the preterm infant's lungs expand during the transition to extrauterine life [1][2]. Both practices enhance oxygenation, blood pressure, and hemoglobin, and reduce risk for ischemia during the switch from placental to pulmonary circulation [3][4].

Research has established that preterm singletons randomized to DCC have lower rates of mortality and morbidity (including intraventricular hemorrhage (IVH)) than newborns who receive early cord clamping [1][5]. Knowledge and practice of DCC are increasing in Canada, but a minority of eligible infants <32 weeks received DCC in 2018 [6]. This statement was developed jointly by obstetric and paediatric experts, based on current best evidence (Figure 1), and updates cord management recommendations made by the Fetus and Newborn Committee of the Canadian Paediatric Society (CPS) in a statement published in 2019 [7]. Guidance includes maternal outcomes, contraindications, and facilitators to improve implementation of DCC and UCM for all infants—but especially preterm infants—in Canada.

Method and approach

A literature search was conducted to capture systematic randomized control trials (RCTs), reviews of RCTs, and observational studies. Searches of Medline, PubMed, Embase and the Cochrane Library from inception to March 2020 were undertaken using Medical Subject Heading (MeSH) terms and key words related to deferred/delayed cord clamping and umbilical cord milking. Guidance is informed by: 1) the Grading of Recommendations,

Assessment, Development and Evaluations (GRADE) Evidence to Decision framework [8]; 2) the Appraisal of Guidelines for Research and Evaluation II Instrument (AGREE II) approach [9]; and 3) the AGREE-Recommendation Excellence (AGREE-REX) tool, which evaluates clinical applicability, values and preferences, and implementability [10].

The benefits of DCC

Preterm singleton births

In the newborn period

DCC decreases mortality by approximately 30% in both extremely preterm infants (gestational age (GA) ≤28 weeks) and preterm infants overall. Two recent meta-analyses of RCTs found a relative risk (RR) of 0.70, 95% confidence interval (CI) 0.51 to 0.95 for extremely preterm infants [5], and an RR of 0.73, 95% CI 0.54 to 0.98 for preterm infants overall [1]. Although the reduction in RR is similar for extremely preterm and all preterm infants, the risks of prematurity decrease substantially over the course of the preterm period. Thus, the absolute benefits of DCC also decrease.

Also, DCC was found to significantly reduce morbidities, including IVH (RR 0.83, 95% CI 0.70 to 0.99 [1]), and necrotizing enterocolitis (NEC) (RR 0.59, 95% CI 0.37 to 0.94) [11]. Infants randomized to DCC had significantly higher mean arterial blood pressure [1] and hematocrit values [5] than those after ICC. DCC also significantly reduced the need for interventions such as blood transfusion (RR 0.66, 95% CI 0.50 to 0.86), and inotropic pressure support (RR 0.37, 95% CI 0.17 to 0.81) [1].

The few adverse side effects with DCC include increased peak bilirubin (mean difference (MD) 4.43 umol/L, 95% CI 1.15 to 7.71 umol/L), and polycythemia in preterm infants overall (RR 2.65, 95% CI 1.61 to 4.37) [5]. However, the need for exchange transfusion [5] or partial exchange transfusion [9] was not significantly increased.

DCC has not been associated with hypothermia, either in systematic reviews of randomized data [1] [5] or in Canadian observational data [6].

Beyond the newborn period

DCC's benefits for singletons extend beyond the neonatal period. A recent meta-analysis of RCTs found that 6 to 10 weeks after preterm birth, DCC slightly increased hematocrit (MD 1.09, 95% CI 0.72 to 1.47) and serum ferritin levels as well (MD 0.38, 95% CI 0.01 to 0.74) [12].

Children born <32 weeks GA who been randomized to DCC for ≥120 seconds (versus ICC) had a reduced risk of death or adverse neurodevelopmental outcomes at 2 years of age (composite outcome, RR 0.61, 95% CI 0.39 to 0.96) [13].

Term singleton births

In the newborn period

The prevalence of hematocrit <45% (study threshold for anemia) has been shown to be significantly lower in infants randomized to receive either 60 or 180 seconds of DCC versus 15 seconds. However, the prevalence of a hematocrit of >65% (study threshold for polycythemia) was significantly higher at 120 seconds (14.1%) than at 15 seconds (4.4%), but not significantly higher than at 60 seconds (5.6%) [14]. The prevalence of neonatal intensive care unit (NICU) admission following 15 seconds, 60 seconds, and 180 seconds of DCC was not significantly different (4.3%, 5.5%, and 8.7%, respectively) [14].

Most RCTs of term infants have focused on longer durations of DCC [15]. A meta-analysis of RCTs noted that term newborns who were randomized to receive DCC up to 60 seconds (versus for longer than 60 seconds, until cessation of cord pulsation) did not experience either improved mortality or morbidity, including NICU admission, while infants receiving DCC up to 60 seconds had slightly lower hemoglobin concentrations (MD - 1.49 g/dL, 95% CI -1.78 to -1.21 g/dL) and significantly lower risk of jaundice requiring phototherapy (RR 0.62, 95% CI 0.41 to 0.96) [15].

Beyond the newborn period

In term singletons, the benefits of DCC beyond the newborn period are demonstrated almost exclusively in RCTs of DCC beyond 60 seconds. These trials have shown significantly improved hemoglobin, iron, ferritin, and transferrin saturation with lower rates of iron deficiency at a variety of time points between 4 to 12 months (RR 0.68, 95% CI 0.49 to 0.94, in a meta-analysis of 20 RCTs) [12].

At 4 years of age, children randomized to DCC (≥180 seconds versus ICC) demonstrated better fine-motor skills and social development scores, although there was no difference in intelligence quotient (IQ) or for 15 other outcomes [16].

Preterm twin births

In the newborn period

There are limited data on cord management in preterm twins, with only one small RCT [17] (80 twins of whom 55 were monochorionic twins) and two cohort studies [18][19]. One meta-analysis found that none of the four trials that included twins stratified outcomes on this basis [5]. A Canadian observational study found some benefits for the 624 twins in total who received DCC, compared with a greater number who received ICC [20]. Although DCC was not associated with a difference in death or severe brain injury occurrence (aOR 1.07, 95% CI 0.78 to 1.47), it was associated with a decrease in need for transfusion (adjusted coefficient -0.49, 95% CI -0.86 to -0.12). DCC was also associated in this study with reduced need for delivery room intubation (aOR 0.53, 95% CI 0.42 to 0.68), mechanical ventilation (adjusted OR 0.51, 95% CI 0.39 to 0.67), and NICU length of stay, (adjusted

coefficient -4.17, 95% CI 8.15 to -0.19) [20] although these findings may relate more to stable infants at birth receiving DCC. In a cohort of twins <32 weeks GA, DCC was associated with significantly lower rates of red blood cell transfusion and surfactant use [18]. No studies stratified outcomes based on whether the twin pregnancies were monochorionic or dichorinonic, although most did not exclude monochorionic twins [17]-[20].

Term twin births

Studies of term twins either have not exclusively focused on twins or did not stratify the data on twins when they were included [15].

Performance of umbilical cord management

Administering uterotonics

Uterotonic medications increase uterine tone to prevent postpartum hemorrhage. They are given prophylactically because they are critical to decreasing maternal morbidity and mortality. However, for preterm infants, there are concerns that using IV uterotonics to prevent postpartum hemorrhage may result in either a bolus effect of transfusion [21] or, conversely, decreased blood flow secondary to uterine contraction [3][22].

Little is known about the impact of uterotonic medications on the infant. One study from the 1960s found that without these medications, blood transfusion to the infant increased from being ~25% complete at 15 seconds, to ~50% at 60 seconds, and ~fully complete at 2 to 3 minutes [21].

The optimal timing to administer prophylactic uterotonics in relation to DCC is not yet clear, ranging in trials from after delivery of the anterior shoulder to after cord clamping [1][15]. One meta-analysis noted that the timing to administer oxytocin by various routes had no significant effect on maternal outcomes, but data remain scant [23]. Subgroup analyses from two meta-analyses based on whether uterotonics were administered before or after DCC [5] [15] found no significant difference in neonatal mortality or morbidity in preterm [6] and term [11] infants, but this result was based on limited data.

Given the potential risk to preterm infants of a bolus effect from transfusion and the lack of adequately powered evidence to suggest optimal timing, prophylactic IV uterotonic medications should be held until after cord clamping in preterm pregnancies [24]. Drug monographs for uterotonics refer to almost immediate onset of action when administered intravenously. It is therefore recommended to hold the administration of uterotonics until after the cord is clamped in preterm pregnancies [25]. Because the onset of intramuscular oxytocin is slower, it may be reasonable to administer this medication without delay or to withhold until cord clamping has occurred, if there is not significant hemorrhage or risk thereof [25]. For term births, when risk for maternal postpartum hemorrhage is greater and the benefits of DCC and the risk of a bolus effect are less, uterotonics should not be deferred, but administered with the anterior shoulder of the final infant delivered.

Duration of DCC

Preterm infants

The optimal duration of DCC has not yet determined, although it is most commonly performed for “at least 60 seconds” [1][5], and can range up to 180 seconds [26]. In preterm infants, one recent Cochrane meta-analysis of 25 RCTs found that deferral ranged from 30 to 59 seconds (10 trials), 60 to 120 seconds (6 trials), greater than 120 seconds (3 trials), and mixed or unknown protocols in 6 trials [1]. For the few trials where DCC was longest, durations were described as beyond 120 seconds in 30 to 36 week GA infants [27], 120 to 180 seconds in infants 29 to 42 weeks GA (mean 38 weeks GA) [28], and 180 seconds in 34 to 36 week GA infants [26]. Despite meta-analysis, an optimal duration for DCC could not be identified.

Ongoing large trials will likely determine whether preterm infants requiring stabilization can benefit from longer durations before clamping. Small studies have demonstrated the feasibility of stabilizing preterm infants with an intact placental circulation for >4 minutes [9], along with similar outcomes on many parameters compared with DCC for 30 to 60 seconds. However, the longer time frame resulted in lower umbilical pH [29], greater risk for hypothermia (48.6%), and much greater risk for hyperbilirubinemia requiring phototherapy (94.6%) [9].

Term infants

In one as meta-analysis of RCTs, term infants receiving DCC for up to 60 seconds (versus >60 seconds, until cord pulsation ceased) had a significantly lower risk of developing jaundice requiring phototherapy (RR 0.62, 95% CI 0.41 to 0.96) [15].

For infants requiring resuscitation, trials have established that providing resuscitation with an intact cord is feasible in both preterm [9][30][31] and term [32] infants. Oxygen saturation and heart rate improved significantly compared with ICC in a mix of late preterm and term infants experiencing respiratory depression at birth [33]. Mean blood pressures and cerebral tissue oxygen saturation also improved when compared with infants who received DCC for 60 seconds without resuscitation on the cord [34]. Larger trials of these findings are underway.

Positioning the infant

Due to low umbilical venous pressures, most trials have positioned the infant using gravity to enhance flow to the infant [3][36]. Studies have warned against elevating the infant, which can impede flow [35]. No trial has yet compared infant outcomes based on positioning [3][36].

Preterm infants

According to one Cochrane meta-analysis of 25 RCTs on DCC in preterm infants, most trials specified that DCC occurred with the infant at or below the level of the introitus or caesarean incision [1]. In another meta-analysis of 27 trials, subgroup analysis did not identify the best position, although numbers were limited [5]. For maintenance of temperature, infants were placed in medical plastic bags, plastic wrap, or warm towels [1]. Preterm infants can be placed on a resuscitation trolley at the maternal bedside, with the cord intact [9][24].

Term infants

In a meta-analysis of RCTs, the positioning of term infants during DCC varied from below the introitus to placenta level to on the mother's abdomen, the last of which typically occurred with DCC $\geq$180 seconds [15]. No clear benefit emerged based on position.

Mode of birth

The effectiveness of DCC after caesarean section has been questioned because uterine surgery can decrease placental transfusion, possibly due to reduced uterine tone [37]-[39]. However, tone is more likely to be an issue at term than in the preterm period. One study found that term infants delivered by caesarean section who received DCC did not experience significant reductions in residual placenta blood volume compared with those receiving ICC or delivered vaginally [39]. Nor did a meta-analysis of RCTs find subgroup differences in infant outcomes based on mode of birth in preterm infants, though data overall were scant [40].

Maternal considerations

There are very limited data on maternal outcomes. Cochrane meta-analyses found no significant differences in either transfusion need (in a single RCT including vaginal birth and caesarean section) or maternal blood loss ($\geq$500 mL, in a single RCT of vaginal birth) after preterm DCC, compared with ICC [1] or term DCC for 60 seconds versus >60 seconds [15]. Data stratifying maternal outcomes by mode of birth are lacking. The same Cochrane review [1] found a single RCT that focused on the effects of UCM on maternal blood loss $\geq$500 mL, but found no such events in either study arm [41]. In twin gestations, there have been conflicting results regarding increased bleeding with DCC [19][42].

Contraindication to DCC

Most infants should receive DCC. In the literature, absolute contraindications to DCC are few but have included the following: fetal hydrops [43], certain fetal anomalies (e.g., diaphragmatic hernia at term) [44], need for immediate resuscitation of mother or infant [43] (except in centres with appropriate experience and equipment to perform resuscitation with an intact cord), or disruption of the placental circulation (e.g., bleeding vasa previa or placenta previa, placental transection or abruption [44][45]). Two trials excluded known cases of twin-to-twin transfusion syndrome, and one excluded monochorionic twins [24][46]. Some, but not all trials excluded cases of IUGR, likely due to an association with polycythemia [41][47]-[49].

Relative contraindications to DCC are few, but include (in term infants) risk factors for significant hyperbilirubinemia (e.g., polycythemia, severe IUGR, pre-gestational diabetes), and cases where maternal antibody titres are high or when the first infant in a pair of monochorionic twins is delivered. In all these circumstances, immediate cord clamping should be considered.

Recent Canadian data for SGA infants <10% and <33 weeks GA have found DCC associated with reduced mortality and severe morbidity (aOR mortality or severe morbidity 0.60, 95% CI 0.42 to 0.86), intubation at birth (aOR 0.29, 95% CI 0.16 to 0.52), inotropic support (aOR 0.47, 95% CI 0.23 to 0.97), IVH (aOR 0.70, 95% CI 0.52 to 0.92), and bronchopulmonary dysplasia (aOR 0.61, 95% CI 0.45 to 0.82) [50]. In a study that did not use DCC, risk for polycythemia increased with the severity of growth restriction (term, non-IUGR infants 6.2%, mild IUGR 8.25%, moderate IUGR 12.5%, severe IUGR 36.2%) [47].

Umbilical cord milking

Preterm infants

One meta-analysis of 5 RCTs found a significant increase in severe IVH in infants $\leq 32^{+6}$ weeks GA with UCM versus DCC (RR 1.95, 95% CI 1.01 to 3.76) [51]. This effect was hypothesized to be related to rapid changes in blood volume.

Term infants

One meta-analysis found only 2 studies comparing UCM to DCC. Both defined DCC as clamping “at or within 30 seconds” [52]. Data are lacking that compare UCM with typically defined DCC in term infants.

Implementation initiatives in Canada

In 2018, the Canadian Preterm Birth Network (CPTBN) and a large, multidisciplinary group of stakeholders (comprising maternal-fetal medicine specialists, obstetricians, neonatologists, paediatricians, nurses, administrators and parents) established a consensus protocol for preterm infants which has informed this statement (see Figure 1). The literature was reviewed and an unpublished draft consensus protocol was created focusing on DCC practice and implementation.

Evidence for improving DCC implementation

Care teams interested in implementing DCC can be informed by a recent systematic review that evaluated strategies, barriers, and facilitators to best practice [54]. The key implementation strategy was to use multidisciplinary “quality improvement approaches” involving “protocols, policies, or toolkits”, education (e.g., rounds, didactic teaching), simulations, and reminders (e.g., signs, newsletters). Occasionally, teams used champions and post-event feedback and debriefing formats [53].

Barriers that teams may need to address include: [53]

1. General change management factors (e.g., lack of staff awareness, resistance to change),
2. Obstetrical care provider concerns (e.g., risk of hemorrhage),
3. Paediatrician concerns (e.g. duration of deferral, polycythemia), and
4. Environmental factors (e.g. bags to minimize infant hypothermia).

Strategies that teams may be able to leverage include: [54]-[57]

1. Guidelines [54][55] or protocols [56],
2. Knowledge of benefits [54][55],
3. Team communication [55], and
4. Reminders [57].

Conclusion

For preterm singletons, DCC reduces risks for mortality and morbidity. For term singletons, DCC improves hematologic parameters. In preterm twins, observational data suggest some benefits. In very preterm infants, UCM doubles the risk of IVH when compared with DCC. There are limited data on preterm twins (with some benefit suggested) and maternal outcomes (no significant reported adverse outcomes). Standardized implementation of DCC practices by a multidisciplinary team should occur for most infants because contraindications to DCC are few. Best practices can be facilitated by reminders, protocols, and team communication. Areas warranting further study include slow UCM, DCC in twins, the timing of uterotonics administration, and the stabilization of preterm infants and resuscitation of preterm or term infants on an intact umbilical cord.

Figure 1. Flow chart for approach to deferred cord clamping (https://cps.ca/uploads/documents/Flow_chart_for_approach_to_deferred_cord_clamping_2.pdf).

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Principal authors: Sarah D McDonald MD, Michael Narvey MD, William Ehman MD, Venu Jain MD PhD, Krista Cassell MD

References

1. Rabe H, Gyte GM, Díaz-Rossello JL, Duley L. Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes. Cochrane Database Syst Revi 2019;9(9):CD003248.
2. WHO. Guideline: Delayed umbilical cord clamping for improved maternal and infant health and nutrition outcomes. Geneva, Switzerland: World Health Organization; 2014.
3. Bhatt S, Polglase GR, Wallace EM, Te Pas AB, Hooper SB. Ventilation before umbilical cord clamping improves the physiological transition at birth. Front Pediatr 2014;2:113.
4. Katheria AC. Neonatal resuscitation with an intact cord: Current and ongoing trials. Children (Basel) 2019;6(4):60.
5. Fogarty M, Osborn D, Askie L, et al. Delayed vs early umbilical cord clamping for preterm infants: A systematic review and meta-analysis. Am J Obstet Gynecol 2018;2018(1):1-18.
6. Beltempo M, Shah P, Yoon EW, Chan P, Balachandran N; Annual Report Review Committee. Annual Report 2018 / Le Réseau Néonatal Canadien 2018 Rapport Annuel (Accessed October 28, 2021).
7. Lee L, Dy J, Azzam H. Management of spontaneous labour at term in healthy women. J Obstet Gynaecol Can 2016;38(9):843-65.
8. Ryan M, Lacaze-Masmonteil T, Mohammad K; Canadian Paediatric Society, Fetus and Newborn Committee. Neuroprotection from acute brain injury in preterm infants (https://cps.ca/documents/position/neuroprotection). Paediatr Child Health 2019;24(4):276-82:
9. Alonso-Coello P, Oxman AD, Moberg J, et al. GRADE Evidence to Decision (EtD) frameworks: A systematic and transparent approach to making well informed healthcare choices. 2: Clinical practice guidelines. BMJ 2016;353:i2089.
10. Brouwer E, Knol R, Vernooij AS, et al. Physiological-based cord clamping in preterm infants using a new purpose-built resuscitation table: A feasibility study. Arch Dis Child Fetal Neonatal Ed 2019;104(4):F396-F402.
11. AGREE-REX Research Team. The Appraisal of Guidelines Research and Evaluation—Recommendation EXcellence (AGREE-REX). 2019: (Accessed October 28, 2021).
12. Garg BD, Kabra NS, Bansal A. Role of delayed cord clamping in prevention of necrotizing enterocolitis in preterm neonates: A systematic review. J MaternFetal Neonatal Med 2019;32(1):164-72.
13. Zhao Y, Hou R, Zhu X, Ren L, Lu H. Effects of delayed cord clamping on infants after neonatal period: A systematic review and meta-analysis. Int J Nurs Stud 2019;92:97-108.
14. Armstrong-Buisseret L, Powers K, Dorling J, et al. Randomised trial of cord clamping at very preterm birth: Outcomes at 2 years. Arch Dis Child Fetal Neonatal Edi 2020;105(3):292-98.
15. Cernadas JMC, Carroli G, Pellegrini L, et al. The effect of timing of cord clamping on neonatal venous hematocrit values and clinical outcome at term: A randomized, controlled trial. Pediatrics 2006;117(4):e779-86.
16. McDonald SJ, Middleton P, Dowswell T, Morris PS. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. Evid Based Child Health 2014;9(2):303-97.
17. Andersson O, Lindquist B, Lindgren M, Stjernqvist K, Domellöf M, Hellström-Westas L. Effect of delayed cord clamping on neurodevelopment at 4 years of age: A randomized clinical trial. JAMA Pediatr 2015;169(7):631-38.
18. Ruangkit C, Bumrunphuet S, Panburana P, Khositseth A, Nuntnarumit P. A randomized controlled trial of immediate versus delayed umbilical cord clamping in multiple-birth infants born preterm. Neonatology 2019;115(2):156-63.
19. Chiruvolu A, Tolia VN, Qin H, et al. Effect of delayed cord clamping on very preterm infants. Am J Obstet Gynecol 2015;213(5):676.e1-7.
20. Liu LY, Yee LM. Delayed cord clamping in preterm dichorionic twin gestations. J Matern Fetal Neonatal Med 2019:1-5.
21. Grabovac M, Beltempo M, Lodha A, et al. Impact of deferred cord clamping in twins: Severe neurologic injury in twins born at <30 weeks of gestation. J Pediatr 2021;238:118-123.e3.
22. Yao AC, Hirvensalo M, Lind J. Placental transfusion-rate and uterine contraction. Lancet. 1968;1(7539)291:380-83.
23. Begley CM, Gyte GM, Devane D, McGuire W, Weeks A, Biesty LM. Active versus expectant management for women in the third stage of labour. Cochrane Database Syst Rev 2019;2(2):CD007412.
24. Soltani H, Hutchon DR, Poulose TA. Timing of prophylactic uterotonics for the third stage of labour after vaginal birth. Cochrane Database Syst Rev 2010;(8):CD006173.
25. Duley L, Dorling J, Pushpa-Rajah A, et al. Randomised trial of cord clamping and initial stabilisation at very preterm birth. Arch Dis Child Fetal Neonatal Ed 2018;103(1):F6-F14.
26. Food and Drug Adminstrition (U.S.). Pitocin. Reference I.D. 3638684. 2014 (Accessed October 29, 2021).
27. Ultee CA, van der Deure J, Swart J, Lasham C, van Baar AL. Delayed cord clamping in preterm infants delivered at 34–36 weeks' gestation: A randomised controlled trial. Arch Dis Child Fetal Neonatal Ed 2008;93(1):F20-F23.

28. Ranjit T, Nesargi S, Suman Rao PN, et al. Effect of early versus delayed cord clamping on hematological status of preterm infants at 6 wk of age. Indian J Pediatr 2015;82(1):29-34.

29. Tiemersma S, Heistein J, Ruijne R, Lopez G, van Lobenstein J, van Rheenen P. Delayed cord clamping in South African neonates with expected low birthweight: A randomised controlled trial. Trop Med Int Health 2015;20(2):177-83.

30. Knol R, Brouwer E, van den Akker T, et al. Physiological-based cord clamping in very preterm infants—Randomised controlled trial on effectiveness of stabilisation. Resuscitation 2020;147:26-33.

31. Pratesi S, Montano S, Ghirardello S, et al. Placental Circulation Intact Trial (PCI-T) – Resuscitation with the placental circulation intact vs. cord milking for very preterm infants: A feasibility study. Front Pediatr 2018;6:364.

32. Winter J, Kattwinkel J, Chisholm C, Blackman A, Wilson S, Fairchild K. Ventilation of preterm infants during delayed cord clamping (VentFirst): A pilot study of feasibility and safety. Am J Perinatol 2017;34(2):111-16.

33. Blank DA, Badurdeen S, Kamlin COF, et al. Baby-directed umbilical cord clamping: A feasibility study. Resuscitation 2018;131:1-7.

34. Andersson O, Rana N, Ewald U, et al. Intact cord resuscitation versus early cord clamping in the treatment of depressed newborn infants during the first 10 minutes of birth (Nepcord III) – A randomized clinical trial. Matern Health Neonatol Perinatol 2019;5:15.

35. Katheria AC, Brown MK, Faksh A, et al. Delayed cord clamping in newborns born at term at risk for resuscitation: A feasibility randomized clinical trial. J Pediatr 2017;187:313-17. e1.

36. Yao AC, Lind J. Effect of gravity on placental transfusion. Lancet 1969;2(7619):505-8.

37. Airey RJ, Farrar D, Duley L. Alternative positions for the baby at birth before clamping the umbilical cord. Cochrane Database Syst Rev 2010;(10):CD007555.

38. Katheria A, Hosono S, El-Naggar W. A new wrinkle: Umbilical cord management (how, when, who). Semin Fetal Neonatal Med 2018;23(5):321-6.

39. Katheria AC, Truong G, Cousins L, Oshiro B, Finer NN. Umbilical cord milking versus delayed cord clamping in preterm infants. Pediatrics 2015;136(1):61-69.

40. Kleinberg F, Dong L, Phibbs RH. Cesarean section prevents placenta-to-infant transfusion despite delayed cord clamping. Am J Obstet Gynecol 1975;121(1):66-70.

41. Elimian A, Goodman J, Escobedo M, Nightingale L, Knudtson E, Williams M. Immediate compared with delayed cord clamping in the preterm neonate: A randomized controlled trial. Obstet Gynecol 2014;124(6):1075-79.

42. Ruangkit C, Leon M, Hassen K, Baker K, Poeltler D, Katheria A. Maternal bleeding complications following early versus delayed umbilical cord clamping in multiple pregnancies. BMC Pregnancy Childbirth. 2018;18(1):131.

43. Rabe H, Wacker A, Hülskamp G, et al. A randomised controlled trial of delayed cord clamping in very low birth weight preterm infants. Eur J Pediatr 2000;159(10):775-77.

44. Dipak NK, Nanavat RN, Kabra NK, Srinivasan A, Ananthan A. Effect of delayed cord clamping on hematocrit, and thermal and hemodynamic stability in preterm neonates: A randomized controlled trial. Indian Pediatr 2017;54(2):112-15.

45. Mercer JS, McGrath MM, Hensman A, Silver H, Oh W. Immediate and delayed cord clamping in infants born between 24 and 32 weeks: A pilot randomized controlled trial. J Perinatol 2003;23(6):466-72.

46. Tarnow-Mordi W, Morris J, Kirby A, et al. Delayed versus immediate cord clamping in preterm infants. N Engl J Med 2017;377(25):2445-55.

47. Kramer MS, Olivier M, McLean FH, Willis DM, Usher RH. Impact of intrauterine growth retardation and body proportionality on fetal and neonatal outcome. Pediatrics 1990;86(5):707-13.

48. Snijders R, Abbas A, Melby O, Ireland RM, Nicolaides KH. Fetal plasma erythropoietin concentration in severe growth retardation. Am J Obstet Gynecol 1993;168(2):615-19.

49. Deorari A, Agarwal R, Paul VK. Management of infants with intra-uterine growth restriction. Indian J Pediatr 2008;75(2):171-74.

50. Brown BE, Shah PS, Afifi JK, et al. Delayed cord clamping in small for gestational age preterm infants. Am J Obstet Gynecol 2021;S0002-9378(21)00867-X.

51. Balasubramanian H, Ananthan A, Jain V, Rao SC, Kabra N. Umbilical cord milking in preterm infants: A systematic review and meta-analysis. Arch Dis Child Fetal Neonatal Ed 2020;105(6):572-80.

52. Al-Wassia H, Shah PS. Efficacy and safety of umbilical cord milking at birth: A systematic review and meta-analysis. JAMA Pediatr 2015;169(1):18-25.

53. Anton O, Jordan H, Rabe H. Strategies for implementing placental transfusion at birth: A systematic review. Birth 2019;46(3):411-27.

54. Devin J, Larkin P. Delayed cord clamping in term neonates: attitudes and practices of midwives in irish hospitals. Int J Childbirth. 2018;8(1):4-17.

55. Perrone B, Ghirardello S. Placental transfusion strategies in Italy: A nationwide survey of tertiary-care delivery wards. Am J Perinatol 2017;34(7):722-28.

56. Oddie S, Rhodes P; Very Preterm Birth Qualitative Collaborative Group. Barriers to deferred cord clamping in preterm infants. Arch Dis Child Fetal Neonatal Ed 2014;99(5):F391-94.

57. Beard MM. PL. 65 Deferred clamping of the umbilical cord: Neural programming in the surgeon as a barrier to change. Arch Dis Child Fetal Neonatal Ed 2013;98(Suppl1):A72-A73.

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