No. 424, March 2022

Guideline No. 424: Umbilical Cord Management in Preterm and Term Infants

(En français : Directive clinique n° 424 : Prise en charge du cordon ombilical chez le nourrisson prématuré ou à terme)

The English document is the original version. In the event of any discrepancy between the English and French content, the English version prevails.

This clinical practice guideline was prepared by the authors and overseen by the SOGC Clinical Practice – Obstetrics Committee and the Canadian Paediatric Society (CPS)'s Fetus and Newborn Committee. It was reviewed by the Association of Ontario Midwives; the Canadian Anesthesiologists' Society; the Canadian Association of Perinatal and Women's Health Nurses; members of the College of Family Physicians of Canada, Advisory Committee on Family Practice and the Maternal and Newborn Care Member Interest Group; the CPS' Community Paediatrics Committee; the SOGC's Maternal Fetal Medicine Committee; the SOGC's Guideline Management and Oversight Committee and approved by the SOGC's Board of Directors and CPS' Board of Directors.

Authors

Sarah D. McDonald, MD, Hamilton, ON
Michael Narvey, MD, Winnipeg, MB
William Ehman, MD, Nanaimo, BC
Venu Jain, MD, PhD, Edmonton, AB
Krista Cassell, MD, Charlottetown, PE

J Obstet Gynaecol Can 2022;44(3):313-322

https://doi.org/10.1016/j.jogc.2022.01.007

SOGC Clinical Practice – Obstetrics Committee (2021): Douglas Black (Chair), Krista Cassell, Mélina Castonguay, Cynthia Chan, Elissa Cohen, Gina Colbourne, Christine Dallaire, Kirsten Duckitt, Sebastian Hobson, Amy Metcalfe, J. Larry Reynolds, Debbie Robinson, Marie-Ève Roy-Lacroix, Kristen Simone, Katherine Tyndall

CPS Fetus and Newborn Committee (2020-2021): Gabriel Altit, Nicole Anderson, Heidi Budden, Leonora Hendson, Souvik Mitra, Michael R. Narvey, Eugene Ng, Nicole Radziminski, Vibhuti Shah

Radha Chari (SOGC Liaison), James Cummings (Committee on Fetus and Newborn, American Academy of Pediatrics Liaison), William Ehman (College of Family Physicians of Canada Liaison), Danica Hamilton (Canadian Association of Neonatal Nurses Liaison), Chloë Joynt (CPS Neonatal-Perinatal Medicine Section Executive Liaison), Chantal Nelson (Public Health Agency of Canada Liaison)

Acknowledgements: The authors would like to thank Kristen Viaje, MD, Hamilton, ON for her assistance with systematic reviews of the literature and drafting of the Figure.

Weeks Gestation Notation: The authors follow the World Health Organization's notation on gestational age: the first day of the last menstrual period is day 0 (of week 0); therefore, days 0 to 6 correspond to completed week 0, days 7 to 13 correspond to completed week 1, etc.

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Disclosures: Statements were received from all authors. No relationships or activities that could involve a conflict of interest were declared. All authors have indicated that they meet the journal's requirements for authorship.

Keywords: umbilical cord; umbilical cord blood; ligation; parturition; time factors; term birth; infant, premature; jaundice, neonatal

Corresponding author: Sarah D. McDonald, mcdonals@mcmaster.ca

KEY MESSAGE

1. Deferred cord clamping benefits most infants, especially preterm infants, and is recommended best practice in most cases. Deferred cord clamping is advised for 60 to 120 seconds with preterm infants, and for 60 seconds with term infants. Umbilical cord milking is not recommended for very preterm infants (<32 weeks).

DEFINITIONS

Preterm: ≤ 37 weeks' gestational age
Very Preterm: < 32 weeks' gestational age
Extremely Preterm: < 28 weeks' gestational age

ABSTRACT

Objective: 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.

Target Population: People who are pregnant with preterm or term singletons or twins.

Benefits, Harms, and 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 increases risk for intraventricular hemorrhage.

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: The authors rated the quality of evidence and strength of recommendations using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. See online Appendix A (Tables A1 for definitions and A2 for interpretations of strong and conditional [weak] recommendations).

Intended Users : Maternity and newborn care providers.

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 deferred (delayed) cord clamping also decrease.

1. Singletons:
   a. In both preterm (<37 weeks) and extremely preterm (<28 weeks) singletons, deferred (delayed) cord clamping 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 deferred (delayed) cord clamping for at least 30 seconds is superior to immediate clamping. Deferred (delayed) cord clamping should be performed with the infant at or below the level of the introitus or at the level of the cesarean incision (*strong, high*).
   b. In term singletons, deferred (delayed) cord clamping is recommended for 60 seconds because it improves hematological outcomes at birth and past the newborn period. Deferred (delayed) cord clamping beyond 60 seconds increases the risk of hyperbilirubinemia requiring phototherapy. Deferred (delayed) cord clamping can be performed with the infant at or below the level of the introitus, or at the level of the cesarean 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 deferred (delayed) cord clamping:
   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, deferred (delayed) cord clamping is associated with some benefits and should be considered, except when contraindicated (*conditional, low*).
   b. In term twins, deferred (delayed) cord clamping may be considered based on presumed extrapolation of benefits in term singletons, except when contraindicated (*conditional, low*).
   c. The evidence regarding optimal duration of deferred (delayed) cord clamping in twins is insufficient. Deferred (delayed) cord clamping for 30 to 60 seconds can be considered (*conditional, low*).
   d. When deferred (delayed) cord clamping 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 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 intravenous uterotonic medications be administered with delivery of the anterior shoulder of the final infant (*conditional, low*).

6. Absolute contraindications to deferred (delayed) cord clamping 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 or twin anemia polycythemia sequence (*strong, high*).
7. Relative contraindications to deferred (delayed) cord clamping are few but include (in term infants) risk factors for significant hyperbilirubinemia (e.g., significant polycythemia, severe intrauterine growth restriction, 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 deferred (delayed) cord clamping are few but include (in preterm infants) risk factors for significant hyperbilirubinemia (e.g., significant polycythemia, severe intrauterine growth restriction, 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 deferred (delayed) cord clamping 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:
    a. Umbilical cord milking is not recommended in very preterm infants $<$32 weeks, due to increased risk for severe intraventricular hemorrhage (*strong, moderate*).
    b. In preterm and term infants, deferred (delayed) cord clamping should be performed instead of umbilical cord milking (*strong, high*).

THE RATIONALE FOR UMBILICAL CORD MANAGEMENT

Best practices for umbilical cord management enhance the transfer of blood from placenta to newborn. Deferred (delayed) 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), and updates cord management recommendations made by the Fetus and Newborn Committee of the Canadian Paediatric Society (CPS) in a statement published in 2019.[8] 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;[9] 2) the Appraisal of Guidelines for Research and Evaluation II Instrument (AGREE II) approach;[10] and 3) the AGREE-Recommendation Excellence (AGREE-REX) tool, which evaluates clinical applicability, values and preferences, and implementability.[11]

ABBREVIATIONS

DCC	deferred (delayed) cord clamping
GA	gestational age
ICC	immediate cord clamping
IVH	intraventricular hemorrhage
IUGR	intrauterine growth restriction
NEC	necrotizing enterocolitis
RCT	randomized controlled trial
SGA	small for gestational age
TAPS	twin anemia polycythemia sequence
TTTS	twin-to-twin transfusion syndrome
UCM	umbilical cord milking

BENEFITS OF DELAYED CORD CLAMPING

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—0.95 for extremely preterm infants,[5] and an RR of 0.73; 95% CI 0.54—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—0.99),[1] and necrotizing enterocolitis (NEC) (RR 0.59; 95% CI 0.37—0.94).[12] 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—0.86), and inotropic pressure support (RR 0.37; 95% CI 0.17—0.81).[1]

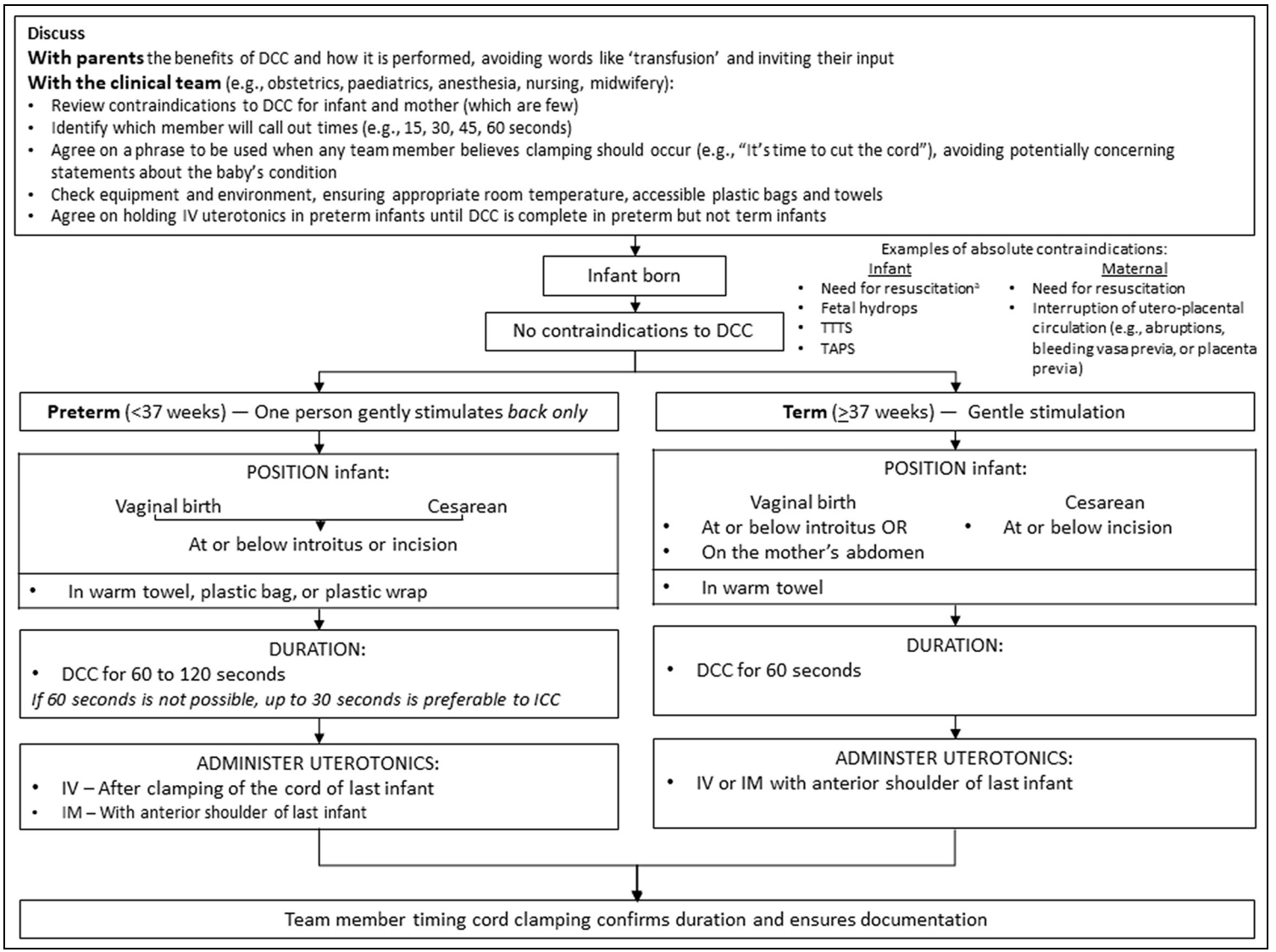
The few adverse side effects with DCC include increased peak bilirubin (mean difference [MD] 4.43 umol/L; 95% CI 1.15—7.71 umol/L), and polycythemia in preterm infants overall (RR 2.65; 95% CI 1.61—4.37).[5] However, the need for exchange transfusion[5] or partial exchange transfusion[10] was not significantly 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

Figure. Flow chart for approach to deferred cord clamping



Note: When DCC is performed with twins, it is suggested that the following 4 individuals be identified: 1) receiving Twin A; 2) monitoring status of Twin A and clamping cord; 3) delivering Twin B; 4) monitoring status of Twin B and clamping cord.
[a]Except in centres with appropriate experience and equipment.
DCC: deferred cord clamping; ICC: immediate cord clamping; IV: intravenous; IM: Intramuscular; TTTS: twin-to-twin transfusion syndrome; TAPS: twin anemia polycythemia sequence.

weeks after preterm birth, DCC slightly increased hematocrit (MD 1.09; 95% CI 0.72−1.47) and serum ferritin levels as well (MD 0.38; 95% CI 0.01− 0.74).[13]

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− 0.96).[14]

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 180 seconds (14.1%) than at 15 seconds (4.4%), but not significantly higher than at 60 seconds (5.9%).[15] 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).[15]

Most RCTs of term infants have focused on longer durations of DCC.[16] 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 0.41−0.96.[16]

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 0.49−0.94, in a meta-analysis of 20 RCTs).[13]

At 4 years of age, children randomized to DCC (≥180 s vs. ICC) demonstrated better fine-motor skills and social development scores, although there was no difference in intelligence quotient (IQ) or for 15 other outcomes.[17]

Preterm Twin Births

In the newborn period

There are limited data on cord management in preterm twins, with only 1 small RCT[18] (80 twins, of whom 55 were monochorionic twins) and 2 cohort studies.[19,20] 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.[21] Although DCC was not associated with a difference in death or severe brain injury occurrence (aOR 1.07; 95% CI 0.78−1.47), 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 0.42−0.68), mechanical ventilation (adjusted OR 0.51; 95% CI 0.39−0.67), and NICU length of stay, (adjusted coefficient −4.17; 95% CI 8.15 to −0.19)[21] 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.[19] No studies stratified outcomes based on whether the twin pregnancies were monochorionic or dichorinonic, although most did not exclude monochorionic twins.[18-21]

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.[16]

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 [22] or, conversely, decreased blood flow secondary to uterine contraction.[3,23]

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.[22]

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.[1,16] One meta-analysis noted that the timing to administer oxytocin by various routes had no significant effect on maternal outcomes, but data remain scant.[24] Subgroup analyses from two meta-analyses based on whether uterotonics were administered before or after DCC[5,16] found no significant difference in neonatal mortality or morbidity in preterm[6] and term[12] 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.[25] 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.[26] 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.[26] 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 Delayed Cord Clamping

Preterm Infants

The optimal duration of DCC has not yet been determined, although it is most commonly performed for "at least 60 seconds",[1,5] and can range up to 180 seconds.[27] 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,[28] 120 to 180 seconds in infants 29 to 42 weeks GA (mean 38 weeks GA),[29] and 180 seconds in 34 to 36 week GA infants.[27] 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,[10] 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,[30] greater risk for hypothermia (48.6%), and much greater risk for hyperbilirubinemia requiring phototherapy (94.6%).[10]

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 0.41−0.96).[16]

For infants who requiring resuscitation, trials have established that providing resuscitation with an intact cord is feasible in both preterm[10,31,32] and term[33] 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.[34] 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.[35] Larger trials of these findings are underway.

Positioning of the Infant

Due to low umbilical venous pressures, most trials have positioned the infant using gravity to enhance flow to the infant.[3,37] Studies have warned against elevating the infant, which can impede flow.[36] No trial has yet compared infant outcomes based on positioning.[3,37]

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 cesarean 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.[10,25]

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 ≥180 seconds.[16] No clear benefit emerged based on position.

MODE OF BIRTH

The effectiveness of DCC after cesarean section has been questioned because uterine surgery can decrease placental

transfusion, possibly due to reduced uterine tone.[38-40] However, tone is more likely to be an issue at term than in the preterm period. One study found that term infants delivered by cesarean section who received DCC did not experience significant reductions in residual placenta blood volume compared with those receiving ICC or delivered vaginally.[40] 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.[7]

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 cesarean section) or maternal blood loss (≥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.[16] 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 ≥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.[20,42]

CONTRAINDICATIONS 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.[25,46] 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 0.42−0.86), intubation at birth (aOR 0.29; 95% CI 0.16−0.52), inotropic support (aOR 0.47; 95% CI 0.23−0.97), IVH (aOR 0.70; 95% CI 0.52−0.92), and bronchopulmonary dysplasia (aOR 0.61; 95% CI 0.45−0.82).[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 ≤32[6] weeks GA with UCM versus DCC (RR 1.95; 95% CI 1.01−3.76).[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). 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.

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APPENDIX A

Table 1. Key to Grading of Recommendations, Assessment, Development and Evaluation Quality of Evidence

Grade	Definition
Strength of recommendation	
Strong	High level of confidence that the desirable effects outweigh the undesirable effects (strong recommendation for) or the undesirable effects outweigh the desirable effects (strong recommendation against)
Conditional [a]	Desirable effects probably outweigh the undesirable effects (weak recommendation for) or the undesirable effects probably outweigh the desirable effects (weak recommendation against)
Quality of evidence	
High	High level of confidence that the true effect lies close to that of the estimate of the effect
Moderate	Moderate confidence in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Limited confidence in the effect estimate: The true effect may be substantially different from the estimate of the effect
Very low	Very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]Do not interpret conditional recommendations to mean weak evidence or uncertainty of the recommendation.

Adapted from GRADE Handbook (2013), Table 5.1.

Table 2. Implications of Strong and Conditional recommendations, by guideline user

Perspective	Strong Recommendation • "We recommend that…" • "We recommend to not…"	Conditional (Weak) Recommendation • "We suggest…" • "We suggest to not…"
Authors	The net desirable effects of a course of action outweigh the effects of the alternative course of action.	It is less clear whether the net desirable consequences of a strategy outweigh the alternative strategy.
Patients	Most individuals in the situation would want the recommended course of action, while only a small proportion would not.	The majority of individuals in the situation would want the suggested course of action, but many would not.
Clinicians	Most individuals should receive the course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that patient choices will vary by individual and that clinicians must help patients arrive at a care decision consistent with the patient's values and preferences.
Policymakers	The recommendation can be adapted as policy in most settings.	The recommendation can serve as a starting point for debate with the involvement of many stakeholders.

Adapted from GRADE Handbook (2013), Table 6.1.