



Toward greater nuance in delayed cord clamping

Laura Marrs^a and Susan Niermeyer^b

Purpose of review

For over a decade, the International Liaison Committee on Resuscitation has recommended delayed cord clamping (DCC), but implementation has been variable due to lack of consensus on details of technique and concerns for risks in certain patient populations. This review summarizes recent literature on the benefits and risks of DCC in term and preterm infants and examines alternative approaches such as physiologic-based cord clamping or intact cord resuscitation (ICR) and umbilical cord milking (UCM).

Recent findings

DCC improves hemoglobin/hematocrit among term infants and may promote improved neurodevelopment. In preterms, DCC improves survival compared to early cord clamping; however, UCM has been associated with severe intraventricular hemorrhage in extremely preterm infants. Infants of COVID-19 positive mothers, growth-restricted babies, multiples, and some infants with cardiopulmonary anomalies can also benefit from DCC. Large randomized trials of ICR will clarify safety and benefits in nonvigorous neonates. These have the potential to dramatically change the sequence of events during neonatal resuscitation.

Summary

Umbilical cord management has moved beyond simple time-based comparisons to nuances of technique and application in vulnerable sub-populations. Ongoing research highlights the importance of an individualized approach that recognizes the physiologic equilibrium when ventilation is established before cord clamping.

Keywords

delayed cord clamping, newborn, physiologic-based cord clamping, placental transfusion, resuscitation, umbilical cord management

INTRODUCTION

For over a decade, the International Liaison Committee on Resuscitation (ILCOR) has recommended delayed cord clamping (DCC) at birth [1]. Despite this, utilization of DCC varies by region, hospital, and patient scenarios [2]. A statewide California quality improvement (QI) collaborative reported inter-hospital variation in DCC from 0 to 74% and only 29% of newborns overall receiving DCC in 2016 [3]. A proliferation of clinical practice guidelines, which differ in their details and sometimes fail to reflect the most recent evidence, may actually add to uncertainty and reluctance to change existing practice [4].

DCC has been most simplistically conceptualized as a timing issue, but many variables impact placental transfusion and cardiopulmonary stability during the immediate transition, the two major goals of DCC. Distribution of blood between the fetus and placenta changes during gestation, and equilibrium after birth may not be achieved as rapidly in preterm infants. The onset of ventilation

exerts a strong influence on circulatory patterns and the volume of placental transfusion, yet the onset of breathing or ventilation in relationship to cord clamping is seldom documented. Failure to breathe may truncate time-based approaches; cord milking may be complete before spontaneous breathing begins, especially in preterms. As evidence builds regarding the crucial role of cord management in safe transition, moving toward greater nuance in understanding how physiological variables and technique influence the process will help

^aUniversity of Colorado School of Medicine and ^bUniversity of Colorado School of Medicine, Colorado School of Public Health, Aurora, Colorado, USA

Correspondence to Susan Niermeyer, MD, MPH, Section of Neonatology, University of Colorado School of Medicine, 13121 E. 17th Avenue, Mail Stop 8402, Aurora, CO 80045, USA. Tel: +1 303 724 2840; e-mail: susan.niermeyer@cuanschutz.edu

Curr Opin Pediatr 2022, 34:170–177

DOI:10.1097/MOP.0000000000001117

KEY POINTS

- Despite accruing evidence for ILCOR's recommendation for DCC, there remains controversy over method and application, and implementation has been variable.
- For term infants, there does not appear to be an association with increased hyperbilirubinemia and there may be neurodevelopmental benefit from the increased iron load from placental transfusion.
- Evidence for survival benefit for preterm infants is increasing and UCM may be mediating an observed increased risk of severe IVH among extremely preterm infants.
- Populations that have historically been excluded from DCC, such as IUGR infants, infants born to COVID-positive mothers, multiples, and those born with cardiopulmonary anomalies have increasing evidence for DCC safety and benefit.
- Future investigation in umbilical cord management, particularly PBCC following ventilation, will be of particular interest to potentially expand the benefits of ICR to nonvigorous infants and has the potential to change delivery room approach significantly.

maximize benefits and minimize any potential undesirable effects of DCC.

Recent large meta-analyses have reaffirmed the major effects of DCC for term and preterm infants; however, these same analyses call attention to the variable approaches and multiple comparisons among these techniques. Often inconclusive results regarding important outcomes leave clinicians wondering what to do. Exploring the nuances that inform management decisions and operationalizing DCC on a case-by-case basis involve examining evidence behind the benefit of DCC in term and preterm infants as well as the potential for undesirable consequences (e.g. exaggerated hyperbilirubinemia) or harm (e.g. intraventricular hemorrhage (IVH)). Alternative approaches, including umbilical cord milking (UCM) and physiologic-based cord clamping (PBCC) or intact-cord resuscitation (ICR), address the issues of depressed newborns needing resuscitation and preterm infants who need respiratory support. Additional considerations include cord management practices amidst a global pandemic and special populations in whom delayed clamping has been controversial, such as growth-restricted infants, multiple gestations, and infants with cardiopulmonary anomalies. Delivering an individualized approach to cord management requires investing effort in implementation at the facility level and continued research to better define technique and outcomes.

BENEFITS OF DELAYED CLAMPING FOR TERM AND NEAR-TERM INFANTS

For term and near-term infants, the immediate benefits of DCC are subtle, and long-term benefits have not yet been persuasively demonstrated; furthermore, data are still limited on cord management for depressed infants. An updated Cochrane review evaluating umbilical cord management included late preterm as well as term infants in 46 studies with comparisons among various methods [5^{*}]. DCC or UCM increased early hemoglobin and hematocrit compared to early cord clamping (ECC) (<30 s); however, the effects were inconclusive for mortality, maternal postpartum hemorrhage (PPH), or anemia in infancy. Wide variability in the methods and definitions of early and delayed clamping across studies likely reduced any difference in observed outcomes; in some studies, infants receiving up to 30 s delay were included in early clamping, and those receiving just over 30 s were analyzed in the delayed clamping group. Methods to promote placental transfusion may increase the use of phototherapy, but notably no standard treatment threshold existed and there was no increase in exchange transfusion. The overall picture of relatively small increments in hematologic values, a suggestion of more hyperbilirubinemia, and inconclusive evidence for long-term outcomes of importance leave some clinicians questioning the value of DCC in this group.

Evidence emerging on improved early physiologic stability and the true incidence of hyperbilirubinemia helps interpret the short-term risk-benefit equation of DCC in term and near-term infants. Term infants realized improved physiologic stability with DCC, including improved heart rate and SpO₂ during the first five minutes after birth [6]. Among healthy term infants, there was no association of hyperbilirubinemia requiring phototherapy with either DCC (2 min) or UCM in a randomized non-inferiority trial [7]. A pre/post comparison after implementation of DCC/UCM among late preterm infants showed a similar incidence of hyperbilirubinemia requiring phototherapy, NICU admission, and readmission for phototherapy [8]. Among another vulnerable group, infants of diabetic mothers, DCC resulted in comparable peak transcutaneous bilirubin and no difference in phototherapy or polycythemia [9]. Assurance that DCC does not result in increased need for treatment of jaundice has special importance in settings where follow-up and phototherapy availability may be limited.

The significance of higher hematocrit and hemoglobin at birth with DCC is hypothesized to lie in improved iron stores in the first months of life, which are essential during a critical window of neurodevelopment. Multiple studies now have

reported increased hemoglobin, ferritin, and mean corpuscular volume in infants between 2 and 12 months who received DCC compared to ECC; many of these were conducted in low- and middle-income countries where rates of iron deficiency are high [10]. Oligodendrocytes, the cells responsible for myelination in the developing brain, are known to be sensitive to iron deprivation. Term infants receiving DCC (5 min) vs. ECC showed increased myelin content in regions of the brain notable for motor function, visual and spatial skills, and sensory processing at 4 and 12 months of age [11[■],12]. There was no difference in developmental assessments between the groups; however, higher Ages and Stages Questionnaires (ASQ) scores in the subdomains of communication and personal-social skills have been identified among 12-month-old term and near-term infants who received DCC, despite no differences in total ASQ scores [13]. The strength of neurodevelopmental studies has been limited due to challenges including protocol violations, loss to follow-up, a variety of assessment tools, and shifting outcomes across age groups [14,15].

BENEFITS OF DELAYED CLAMPING FOR PRETERM INFANTS

For preterm infants, there is evidence of improved hemoglobin and hematocrit, reduction in the use of inotropes and transfusion, and even improved survival with DCC, though the exact mechanisms underlying this effect remain uncertain. Several meta-analyses have now supported improved survival for preterm infants with DCC compared to ECC, including an updated Cochrane review that suggested a trend from no difference in survival to slightly improved survival with longer delay (Fig. 1) [16–18,19[■]]. These analyses report variable reduction of complications such as IVH, necrotizing enterocolitis, and anemia of prematurity. Although the exact mechanism of improved survival remains unclear, both improved cardiopulmonary stability in the immediate postnatal transition and improved blood volume likely play a role. There may be mechanical interactions of a replete blood volume with endothelial cells that promote healthy organ development as well as homeostatic benefits [11[■],20]. Despite the potential for improved survival,

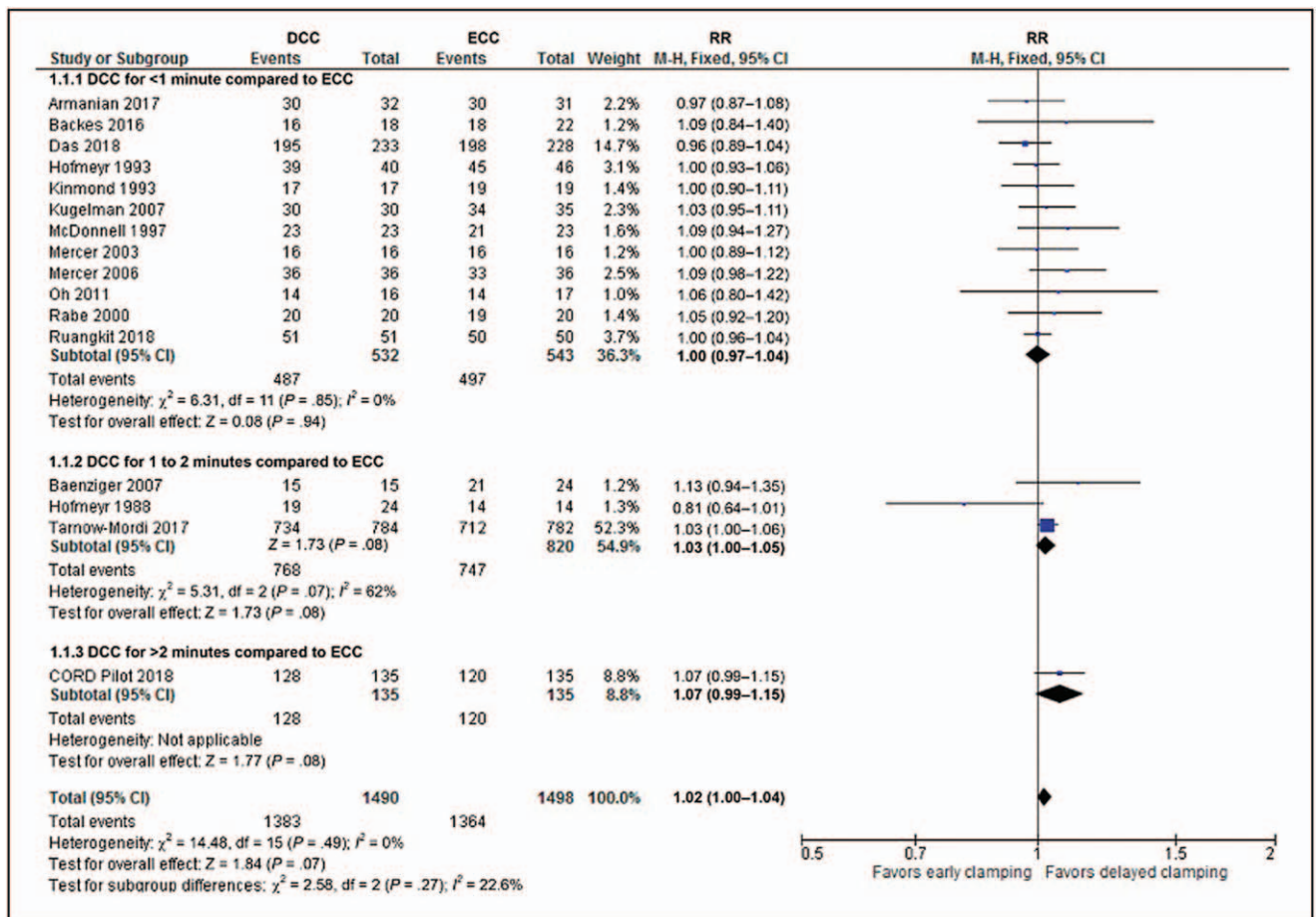


FIGURE 1. Forest plot of DCC vs ECC demonstrating survival to hospital discharge. Reprinted with permission from Seidler *et al.* [19[■]]. DCC, delayed cord clamping; ECC, early cord clamping.

the most immature infants are least likely to receive this intervention [21].

UMBILICAL CORD MILKING

UCM offers rapid intervention to accomplish placental transfusion; however, its usefulness in depressed infants or those with compromised uteroplacental circulation remains uncertain and concerning evidence exists relative to increased severe IVH in extremely preterm infants. Two meta-analyses of UCM compared to DCC have shown comparable early hematological outcomes in term and late-preterm vigorous neonates [22,23]. Most studies evaluating the use of UCM have not employed it for situations in which DCC is currently contraindicated.

UCM is especially attractive at preterm birth to quickly move the infant to receive respiratory support, but concern has grown that the rapid bolus of blood and fluctuating cerebral blood flow may mediate severe IVH among extremely preterm infants. This is especially evident when UCM is compared to DCC and was supported in two recent meta-analyses, a randomized controlled trial (RCT), and additional multicenter retrospective studies [24,25,26*,27,28*]. This effect may have previously been obscured in comparisons of UCM vs. ECC, also a potential risk factor for IVH.

There has been no significant decrease in mortality identified in comparisons of UCM vs. ECC [18,29]. One meta-analysis comparing UCM to both ECC and DCC in < 37-week preterm infants found the additional risk of RDS with UCM [30]. These analyses are complicated by variable times to onset of breathing and different UCM strategies, resulting in differential placental transfusion and stability of cerebral perfusion. For extremely preterm infants, DCC as compared to UCM consistently shows improved mortality and a better safety profile in regard to severe IVH. To avoid UCM risks in the nonvigorous infant, studies of ICR are urgently needed for this population.

PHYSIOLOGIC-BASED CORD CLAMPING AND INTACT CORD RESUSCITATION

PBCC, with clamping after breathing and respiratory stability, and ICR, in which assisted ventilation is provided with cord intact, have been shown to facilitate smooth cardiopulmonary transition and placental transfusion in feasibility trials (Fig. 2). Clamping after the onset of respirations or the provision of respiratory support avoids reflex bradycardia, compensatory tachycardia and swings in blood pressure and flow. Physiologic endpoints emphasize

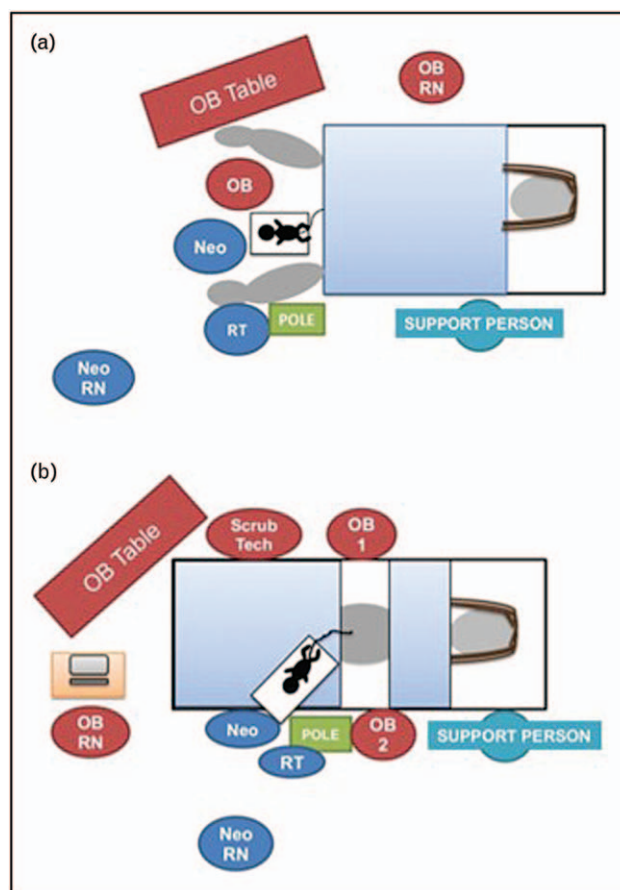


FIGURE 2. Example of resuscitation team and equipment locations during an ICR trial for (a) vaginal delivery and (b) caesarean section. The referenced pole was mobile and contained a T-piece resuscitator. Reprinted with permission from Foglia *et al.* [69].

equilibration and more complete transfer of respiratory function from the placenta to the lungs of the infant.

Pilot trials of ICR, such as Baby-DUCC in non-vigorous term and moderately preterm infants, have demonstrated feasibility and safety [31]. Nepcord III showed improved Apgar score and SpO₂ at one, five, and ten minutes of life among late preterm and term infants who received ICR vs. ECC [32*]. Although most infants require only ventilation to support a successful transition, a small minority require chest compressions. An ovine model showed return of spontaneous circulation is possible with ICR and suggested a benefit in reducing postasphyxial hypertension with the low-pressure placental circuit intact [33].

The hemodynamic implications of maintaining cardiac preload via placental transfusion and relatively low afterload on the low-pressure placental circuit are very important to the preterm population. Data from asphyxiated preterm lambs show

improved ventilation and pulmonary blood flow with ICR [34]. A large noninferiority trial randomized preterm infants to PBCC with clamping after ventilatory support and establishment of spontaneous breathing with vital sign stability vs. the standard 30–60 s delay. Infants receiving PBCC showed decreased time to clinical stability, but no other significant differences for maternal or short-term neonatal outcome [35^{***}].

PBCC also aids thermoregulation through continued perfusion with warm placental blood, as evidenced in a lamb model [36]. Simultaneous placement of plastic wrap during DCC is associated with decreased time to initiate respiratory support and longer maintenance of placental circulation, demonstrating that it is feasible to begin additional thermoregulation techniques whereas facilitating placental transfusion [37]. The practice of PBCC supports the triad of immediate delivery room necessity: ventilation, placental transfusion, and thermoregulation. This has an important clinical implication, as hypothermia in the preterm infant continues to be implicated as an independent risk factor for increased mortality [38].

The neurodevelopmental outcome for preterm infants at 2 years from the Cord Pilot Trial of ICR (2 min) vs. ECC showed a decreased risk of death or adverse neurologic outcome with ICR. This study is of special import given the preterm population that was studied, with a median gestational age of 29 weeks, and the inclusion of infants who required immediate resuscitative efforts [39].

A survey of practice in the UK revealed a significant portion of neonatal intensive care units planning to implement ICR for preterm infants, but cited delays in education on the practice and supporting equipment to be barriers [40]. To assist with ICR, multiple resuscitation platforms have been developed and adapted to the limited physical space for resuscitation [41–45]. Other solutions address cost-effective methods suitable for low-resource settings [46]. Novel monitoring devices, such as a dry electrode electrocardiogram belt and a wireless cap heart rate monitor, may provide reassurance regarding clinical status during the process of ICR [47,48].

SPECIAL CONSIDERATIONS

Cord management and COVID-19

Early in the COVID-19 pandemic, uncertainty about vertical transmission from mother to fetus/newborn and lack of adequate protection for healthcare workers attending deliveries led to some, though not universal, calls for ECC [49–52]. As experience accumulated, evidence suggested that perinatal

transmission occurred most often through respiratory spread, with no apparent contribution from DCC [53]. Two prospective observational registry studies demonstrated safety of DCC and immediate skin-to-skin contact in SARS-CoV-2 positive mothers [54,55]. Policy statements from the American Academy of Pediatrics have evolved from initial consideration of separation of a SARS-CoV-2-positive mother and infant to reaffirmation of DCC as the standard of care [56]. Keeping mother and baby together supports not only DCC but also other goals of the immediate newborn period, including breastfeeding and skin-to-skin care.

Intrauterine growth restriction

Growth restriction is often questioned as a reason for exclusion from DCC because of concerns around polycythemia in the fetus, placental function at delivery, and hemodynamics of placental transfusion with abnormal umbilical artery flow [2,57]. A randomized trial of DCC vs. ECC in vigorous growth-restricted neonates ≥ 28 weeks gestation demonstrated improved SVC flow, comparable phototherapy durations, and no change in the incidence of polycythemia [58^{*}]. Among < 34 -week vigorous newborns with placental insufficiency documented by abnormal Doppler indices, greater than 60 s of DCC was associated with increased stem cell transfusion, lower need for red cell transfusion, and decreased anemia at 2 months in another RCT [59^{*}]. Further corroborating these findings, a large retrospective cohort study of infants < 33 weeks gestation from the Canadian Neonatal Network separated those who had received < 30 or ≥ 30 s of delay and identified a significant improvement in mortality and preterm morbidities in the delayed clamping group without a difference between the groups in peak bilirubin level [60^{*}]. DCC appears safe for growth-restricted neonates, but merits collaboration and planning for umbilical cord management with obstetric colleagues and careful monitoring of the baby at delivery.

Multiple gestations

Twins and higher-order multiples are often excluded from delayed clamping, but the prevalence of prematurity and potential benefit of DCC have brought attention to this population [2]. The study of cord management in multiples is complicated by the effect of birth order, inter-twin vascular connections in monochorionic twins, and concern for acute maternal hemorrhage. A large retrospective cohort of twins demonstrated a significant difference in initial hemoglobin between both mono- and dichorionic twin pairs born by vaginal delivery, with

twin B having higher hemoglobin. There was no evidence for acute intertwin hemorrhage, and the observed difference was ascribed to differential clamping times [61]. A retrospective observational study showed that multiples less than 33 weeks gestation of mono/di/and tri chorionicity receiving DCC had similar outcomes to singletons receiving DCC [62]. In an RCT of preterm multiples between 28–36 weeks gestation, there was no difference in admission hematocrit between early and delayed clamping groups, but more frequent PPH in the DCC group, which contradicts other studies [63–65]. In a retrospective registry study from the National Institute of Child Health and Human Development Neonatal Research Network, 19% of the cohort < 29 weeks were twins; those who received placental transfusion had lower odds of mortality [66]. Another large database study from the Canadian Neonatal/Preterm Birth Network did not uncover significant differences in death and/or severe neurologic injury between twins who underwent DCC vs. ECC, though DCC was associated with decreased transfusions and length of stay [67]. Strong evidence has not surfaced to avoid DCC in multiples, and given the risks of prematurity and the evidence for decreased mortality, DCC should be considered in this population.

Cardiopulmonary abnormalities and extreme immaturity

Other populations at risk for immediate respiratory insufficiency at birth, including those with congenital diaphragmatic hernia, hydrops fetalis, and extreme prematurity, may benefit from prolonged use of the placental circuit. ICR has been performed in infants with pleural effusion secondary to hydrops [68]. Additionally, ICR has been investigated in a feasibility trial among infants with isolated congenital diaphragmatic hernia [69]. A multicenter RCT is currently enrolling to evaluate for efficacy of cardiorespiratory adaptation between ICR and ECC in this population [70]. Another growing population of interest is neonates under 24 weeks gestation, who were determined in a retrospective study to have significantly decreased early mortality when provided with placental transfusion [66]. ICR may act as a biologic safety net that supports safe transition in a growing list of clinical situations that were previously regarded as exclusions.

OVERCOMING CHALLENGES TO IMPLEMENTATION

Effecting change in behavior to provide DCC requires deliberate strategies for implementation,

especially when the practice does not have perceived benefit to practitioners or health systems in terms of time or money. QI strategies have proven to be especially useful to promote implementation, as this approach incorporates evidence review, addresses concerns of obstetrical and pediatric clinicians, formulates an agreed-upon management plan, and monitors outcomes of interest. Recent examples include the implementation of a delivery room QI bundle including DCC, which was associated with reduced rates of mechanical ventilation during NICU admission of infants <32 weeks [71]. Using simulation to introduce mobile resuscitation equipment in the delivery room essentially eliminated ECC in term and near-term vaginal deliveries at another site [72]. QI initiatives have also been helpful in resource-constrained settings to increase rates of DCC [73].

The release of the Neonatal Resuscitation Program 8th edition (NRP 8) with revision of the pre-delivery questions to include a multidisciplinary prebrief on umbilical cord management provides an opportunity for medical teams to discuss and plan for this important decision at each birth [74]. NRP 8 advises against UCM in <28-week infants, but now notes, ‘if the placental circulation is intact, it may be reasonable to briefly delay cord clamping,’ which allows for the initial steps of drying, stimulation to breathe, and clearing the airway to take place with an intact cord [74]. Stimulation of noncrying infants with cord intact decreased the use of bag-and-mask ventilation to 18% as compared to 32% among noncrying infants whose cords were clamped immediately [75]. Such an approach provides an interim solution whereas awaiting the results of large trials of ICR in depressed newborns.

CONCLUSION AND DIRECTIONS FOR FUTURE RESEARCH

Future inquiry into umbilical cord management is now at an inflection point. It has moved beyond comparisons with early clamping to examine methods that address the individual needs of specific populations of infants to optimize beneficial effects. In future studies, it will be critical to standardize interventions, document when an infant is successfully ventilated in relation to umbilical cord clamping and aim to collect a core set of standardized outcome measures in order to interpret these nuanced comparisons. Innovative functional physiologic methods to monitor neurodevelopment and continued studies of long-term neurodevelopmental outcomes could strengthen the rationale for delayed clamping. The results of ongoing large RCTs of PBCC (ABC trial, *VentFirst*, *Baby-DUCC*) will be of

particular interest for those infants who may benefit from ICR. Whatever direction these studies and others guide the science of resuscitation, it will take collaborative efforts from teams caring for baby and mother to individualize cord management and ensure that our first act of caring for our most vulnerable maximizes benefit and indeed does no harm.

Acknowledgements

None.

Financial support and sponsorship

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Perلمان JM, Wyllie J, Kattwinkel J, *et al.* Part 11: Neonatal resuscitation: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation* 2010; 122(16 Suppl 2):S516–S538.
2. Chiruvolu A, Mallett LH, Govande VP, *et al.* Variations in umbilical cord clamping practices in the United States: a national survey of neonatologists. *J Matern Fetal Neonatal Med* 2020; 1–7. doi: 10.1080/14767058.2020.1836150.
3. Tran CL, Parucha JM, Jegatheesan P, Lee HC. Delayed cord clamping and umbilical cord milking among infants in California neonatal intensive care units. *Am J Perinatol* 2020; 37:151–157.
4. Liyanage SK, Ninan K, McDonald SD. Guidelines on deferred cord clamping and cord milking: a systematic review. *Pediatrics* 2020; 146:e20201429.
5. Gomersall J, Berber S, Middleton P, *et al.* Umbilical cord management at term and late preterm birth: a meta-analysis. *Pediatrics* 2021; 147:e2020015404. Cochrane systematic review and meta-analysis comparing the range of approaches to umbilical cord management in term and near-term infants.
6. Padilla-Sanchez C, Baixauli-Alacreu S, Canada-Martinez AJ, *et al.* Delayed vs immediate cord clamping changes oxygen saturation and heart rate patterns in the first minutes after birth. *J Pediatr* 2020; 227:149–156 e1.
7. Seliga-Siwecka JP, Puskasz-Gasowska J, Tolloczko J. The risk of hyperbilirubinemia in term neonates after placental transfusion - a randomized-blinded controlled trial. *Ginekol Pol* 2020; 91:613–619.
8. Chiruvolu A, George R, Stanzo KC, *et al.* Effects of placental transfusion on late preterm infants admitted to a mother baby unit. *Am J Perinatol* 2021. doi: 10.1055/s-0041-1726387. [Epub ahead of print]
9. Bennett C, Munoz JL, Yao M, Singh K. Effects of delayed cord clamping on neonatal hyperbilirubinemia in pregestational diabetes at term. *J Matern Fetal Neonatal Med* 2021; 1–9. doi: 10.1080/14767058.2021.1946785.
10. Fu X, Dang D, Li S, *et al.* Effect of delayed versus early cord clamping on improving anemia in term infants aged two months or older – a meta-analysis. *Indian Pediatr* 2020; 57:815–819.
11. Mercer JS, Erickson-Owens DA, Deoni SCL, *et al.* The effects of delayed cord clamping on 12-month brain myelin content and neurodevelopment: a randomized controlled trial. *Am J Perinatol* 2022; 39:037–044. RCT demonstrating increased white matter brain growth among term infant at 12 months, providing insight into potential mechanisms linking iron stores and neurodevelopment.
12. Mercer JS, Erickson-Owens DA, Deoni SCL, *et al.* Effects of delayed cord clamping on 4-month ferritin levels, brain myelin content, and neurodevelopment: a randomized controlled trial. *J Pediatr* 2018; 203:266–272 e2.
13. Xodo S, Xodo L, Baccarini G, *et al.* Does delayed cord clamping improve long-term (≥ 4 months) neurodevelopment in term babies? A systematic review and a meta-analysis of randomized clinical trials. *Front Pediatr* 2021; 9:651410. doi: 10.3389/fped.2021.651410.
14. Isacson M, Gurung R, Basnet O, *et al.* Neurodevelopmental outcomes of a randomised trial of intact cord resuscitation. *Acta Paediatr* 2021; 110:465–472.
15. Taylor GL, Joseph RM, Kuban KCK, *et al.* Changes in neurodevelopmental outcomes from age 2 to 10 years for children born extremely preterm. *Pediatrics* 2021; 147:e2020001040.
16. Li J, Yang S, Yang F, *et al.* Immediate vs delayed cord clamping in preterm infants: a systematic review and meta-analysis. *Int J Clin Pract* 2021; 75:e14709.
17. Fogarty M, Osborn DA, Askie L, *et al.* Delayed vs early umbilical cord clamping for preterm infants: a systematic review and meta-analysis. *Am J Obstet Gynecol* 2018; 218:1–18.
18. Jasani B, Torgalkar R, Ye XY, *et al.* Association of umbilical cord management strategies with outcomes of preterm infants: a systematic review and network meta-analysis. *JAMA Pediatr* 2021; 175:e210102.
19. Seidler AL, Gyte GML, Rabe H, *et al.* Umbilical cord management for newborns <34 weeks' gestation: a meta-analysis. *Pediatrics* 2021; 147:e20200576. Cochrane systematic review and meta-analysis comparing the range of approaches to umbilical cord management in preterm infants.
20. Mercer JS, Erickson-Owens DA, Rabe H. Placental transfusion: may the 'force' be with the baby. *J Perinatol* 2021; 41:1495–1504.
21. Singh N, Brammer D. Delayed cord clamping in infants born less than 35 weeks: a retrospective study. *J Neonatal Perinatal Med* 2021; 14:391–395.
22. Jeevan A, Ananthan A, Bhuwan M, *et al.* Umbilical cord milking versus delayed cord clamping in term and late-preterm infants: a systematic review and meta-analysis. *J Matern Fetal Neonatal Med* 2021; 1–11. doi: 10.1080/14767058.2021.1884676.
23. Fuwa K, Tabata N, Ogawa R, *et al.* Umbilical cord milking versus delayed cord clamping in term infants: a systematic review and meta-analysis. *J Perinatol* 2021; 41:1549–1557.
24. Balasubramanian H, Ananthan A, Jain V, *et al.* Umbilical cord milking in preterm infants: a systematic review and meta-analysis. *Arch Dis Child Fetal Neonatal Ed* 2020; 105:572–580.
25. Katheria AC, Szychowski JM, Essers J, *et al.* Early cardiac and cerebral hemodynamics with umbilical cord milking compared with delayed cord clamping in infants born preterm. *J Pediatr* 2020; 223:51–56 e1.
26. Kumbhat N, Eggleston B, Davis AS, *et al.* Umbilical cord milking vs delayed cord clamping and associations with in-hospital outcomes among extremely premature infants. *J Pediatr* 2021; 232:87–94 e4. Retrospective cohort study from NICHD Neonatal Research Network demonstrating an association of severe intraventricular hemorrhage with umbilical cord milking as compared to DCC
27. Sanchez-Ramos L, Cullough DM, Mitta M, *et al.* Does umbilical cord milking increase the risk of severe intraventricular hemorrhage in extreme preterm neonates? A multitreatment comparison. *Am J Obstet Gynecol* 2020; 223:590–592.
28. El-Naggar W, Afifi J, Dorling J, *et al.* A comparison of strategies for managing the umbilical cord at birth in preterm infants. *J Pediatr* 2020; 225:58–64 e4. Retrospective cohort study from the Canadian Neonatal Network demonstrating an association of severe intraventricular hemorrhage with umbilical cord milking as compared to DCC
29. Barboza JJ, Albitres-Flores L, Rivera-Meza M, *et al.* Short-term efficacy of umbilical cord milking in preterm infants: systematic review and meta-analysis. *Pediatr Res* 2021; 89:22–30.
30. Ortiz-Esquinas I, Gomez-Salgado J, Rodriguez-Almagro J, *et al.* Umbilical cord milking in infants born at <37 weeks of gestation: a systematic review and meta-analysis. *J Clin Med* 2020; 9:1071.
31. Blank DA, Badurdeen S, Omar FKC, *et al.* Baby-directed umbilical cord clamping: a feasibility study. *Resuscitation* 2018; 131:1–7.
32. 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 min of birth (Nepcord III) – a randomized clinical trial. *Matern Health Neonatal Perinatol* 2019; 5:15. RCT demonstrating higher saturations, earlier onset of breathing and regular breathing among infants with intact cord resuscitation.
33. Polglase GR, Schmolzer GM, Roberts CT, *et al.* Cardiopulmonary resuscitation of asystolic newborn lambs prior to umbilical cord clamping; the timing of cord clamping matters! *Front Physiol* 2020; 11:902.
34. Chandrasekharan P, Gugino S, Helman J, *et al.* Resuscitation with an intact cord enhances pulmonary vasodilation and ventilation with reduction in systemic oxygen exposure and oxygen load in an asphyxiated preterm ovine model. *Children (Basel)* 2021; 8:307.
35. 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. RCT noninferiority study demonstrating effectiveness of stabilization of very preterm infants with PBCC
36. Blank DA, Crossley KJ, Kashyap AJ, *et al.* Physiologic-based cord clamping maintains core temperature vs. immediate cord clamping in near-term lambs. *Front Pediatr* 2020; 8:584983.
37. Engle W, Lien I, Benneyworth B, *et al.* Placental transfusion, timing of plastic wrap or bag placement, and preterm neonates. *Am J Perinatol* 2021. doi: 10.1055/s-0041-1730437.

38. Dubos C, Querne L, Brenac W, Tourneux P. Association between hypothermia in the first day of life and survival in the preterm infant. *Arch Pediatr* 2021; 28:197–203.
39. 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 Ed* 2020; 105:292–298.
40. Bean AE, Myers L, Smith C, Williams T. Intact cord stabilisation and delivery room strategies: current practice in the UK. *Arch Dis Child Fetal Neonatal Ed* 2021; 106:569–570.
41. Katheria A, Lee HC, Knol R, *et al*. A review of different resuscitation platforms during delayed cord clamping. *J Perinatol* 2021; 41:1540–1548.
42. Katheria AC, Allman P, Szychowski JM, *et al*. Perinatal outcomes of subjects enrolled in a multicenter trial with a waiver of antenatal consent. *Am J Perinatol* 2020. doi:10.1055/s-0040-1719184.
43. Hutcheon D, Pratesi S, Katheria A. How to provide motherside neonatal resuscitation with intact placental circulation? *Children* 2021; 8:291.
44. Joshi NS, Padua K, Sherman J, *et al*. A feasibility study of a novel delayed cord clamping cart. *Children* 2021; 8:357.
45. UshaDevi R, Mangalabharathi S, Prakash V, *et al*. Delivery room care and neonatal resuscitation while on intact placental circulation: an open-label, single-arm study. *J Perinatol* 2021; 41:1558–1565.
46. Ditai J, Barry A, Burgoine K, *et al*. The babysaver: design of a new device for neonatal resuscitation at birth with intact placental circulation. *Children* 2021; 8:526.
47. Bush JB, Cooley V, Perlman J, Chang C. NeoBeat offers rapid newborn heart rate assessment. *Arch Dis Child Fetal Neonatal Ed* 2021; 106:550–552.
48. Henry C, Shipley L, Ward C, *et al*. Accurate neonatal heart rate monitoring using a new wireless, cap mounted device. *Acta Paediatr* 2021; 110:72–78.
49. Fan S, Yan S, Liu X, *et al*. Human coronavirus infections and pregnancy. *Matern Fetal Med* 2021; 3:53–65.
50. Geffner SC, Avila AS, Etcharran ML, *et al*. Preparedness strategies in neonatology units during the COVID-19 pandemic: a survey conducted at maternity centers in Argentina. *Arch Argent Pediatr* 2021; 119:76–82.
51. Shahbazi Sigaldehy S, Ebrahimi Kalan M. Care of newborns born to mothers with COVID-19 infection; a review of existing evidence. *J Matern Fetal Neonatal Med* 2020; 1–13. doi:10.1080/14767058.2020.1777969.
52. Vogel JP, Tendal B, Giles M, *et al*. Clinical care of pregnant and postpartum women with COVID-19: living recommendations from the National COVID-19 Clinical Evidence Taskforce. *Aust N Z J Obstet Gynaecol* 2020; 60:840–851.
53. Kollikonda S, Chavan M, Cao C, *et al*. Transmission of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) through infant feeding and early care practices: A systematic review. *J Neonatal Perinatal Med* 2021.
54. Mejia Jimenez I, Salvador Lopez R, Garcia Rosas E, *et al*. Umbilical cord clamping and skin-to-skin contact in deliveries from women positive for SARS-CoV-2: a prospective observational study. *BJOG* 2021; 128:908–915.
55. Sanchez-Luna M, Fernandez Colomer B, de Alba Romero C, *et al*. Neonates born to mothers with COVID-19: data from the Spanish Society of Neonatology Registry. *Pediatrics* 2021; 147:e2020015065.
56. Flannery DD, Puopolo KM. Perinatal COVID-19: guideline development, implementation, and challenges. *Curr Opin Pediatr* 2021; 33:188–194.
57. Bruckner M, Katheria AC, Schmolzer GM. Delayed cord clamping in healthy term infants: more harm or good? *Semin Fetal Neonatal Med* 2021; 26:101221.
58. Dugal KC, Singh P, Srivastava Y, *et al*. Effects of delayed cord clamping in ■ intrauterine growth-restricted neonates: a randomized controlled trial. *Eur J Pediatr* 2021; 180:1701–1710.
- RCT demonstrating increased superior vena cava flow, hematocrit and ferritin with DCC but no increase in polycythemia or duration of phototherapy
59. Yunis M, Nour I, Gibreel A, *et al*. Effect of delayed cord clamping on stem cell ■ transfusion and hematological parameters in preterm infants with placental insufficiency: a pilot randomized trial. *Eur J Pediatr* 2021; 180:157–166.
- RCT demonstrating increased transfusion of stem cells with decreased anemia and transfusion need among preterm infants with placental insufficiency
60. Brown BE, Shah PS, Afifi JK, *et al*. Delayed cord clamping in small for ■ gestational age preterm infants. *Am J Obstet Gynecol* 2021; 226: 247.e1–247.e10.
- Retrospective cohort study from the Canadian Neonatal Network demonstrating an association of DCC with reduction in a composite outcome of mortality or major morbidity.
61. Verbeek L, Zhao DP, Middeldorp JM, *et al*. Haemoglobin discordances in twins: due to differences in timing of cord clamping? *Arch Dis Child Fetal Neonatal Ed* 2017; 102:F324–F328.
62. Jegatheesan P, Belogolovsky E, Nudelman M, *et al*. Neonatal outcomes in preterm multiples receiving delayed cord clamping. *Arch Dis Child Fetal Neonatal Ed* 2019; 104:F575–F581.
63. Ruangkit C, Bumrunghuet S, Panburana P, *et al*. A Randomized controlled trial of immediate versus delayed umbilical cord clamping in multiple-birth infants born preterm. *Neonatology* 2019; 115:156–163.
64. Ruangkit C, Leon M, Hassen K, *et al*. Maternal bleeding complications following early versus delayed umbilical cord clamping in multiple pregnancies. *BMC Pregnancy Childbirth* 2018; 18:131.
65. McDonald SJ, Middleton P, Dowswell T, Morris PS. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. *Cochrane Database Syst Rev* 2013; 2013:CD004074.
66. Kumbhat N, Eggleston B, Davis AS, *et al*. Placental transfusion and short-term outcomes among extremely preterm infants. *Arch Dis Child Fetal Neonatal Ed* 2021; 106:62–68.
67. Grabovac M, Beltempo M, Lodha A, *et al*. Impact of deferred cord clamping on mortality and severe neurologic injury in twins born at <30 weeks of gestation. *J Pediatr* 2021; 238:118–123 e3.
68. Comert HSY, Kader S, Osmanagaoglu MA, *et al*. Prenatal and postnatal management of intrauterine pleural effusions associated with nonimmune hydrops fetalis. *Am J Perinatol* 2020. doi:10.1055/s-0040-1721689.
69. Foglia EE, Ades A, Hedrick HL, *et al*. Initiating resuscitation before umbilical cord clamping in infants with congenital diaphragmatic hernia: a pilot feasibility trial. *Arch Dis Child Fetal Neonatal Ed* 2020; 105:322–326.
70. Le Duc K, Mur S, Rakza T, *et al*. Efficacy of intact cord resuscitation compared to immediate cord clamping on cardiorespiratory adaptation at birth in infants with isolated congenital diaphragmatic hernia (CHIC). *Children* 2021; 8:339.
71. Lo SC, Bhatia R, Roberts CT. Introduction of a quality improvement bundle is associated with reduced exposure to mechanical ventilation in very preterm infants. *Neonatology* 2021; 118:578–585.
72. Saether E, Reinhart-Van Gulpen F, Jensen C, *et al*. Neonatal transitional support with intact umbilical cord in assisted vaginal deliveries: a quality-improvement cohort study. *BMC Pregnancy Childbirth* 2020; 20:496.
73. Sachan R, Srivastava H, Srivastava S, *et al*. Use of point of care quality improvement methodology to improve newborn care, immediately after birth, at a tertiary care teaching hospital, in a resource constraint setting. *BMJ Open Qual* 2021; 10(Suppl 1):e001445.
74. Weiner G, Zaichkin J, editors. *Textbook of Neonatal Resuscitation*. 8th ed. Itasca, IL: American Academy of Pediatrics; 2021, 361 pp.
75. KC A, Budhathoki SS, Thapa J, *et al*. Impact of stimulation among noncrying neonates with intact cord versus clamped cord on birth outcomes: observation study. *BMJ Paediatr Open* 2021; 5:e001207.