



Delayed cord clamping-the evidence

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- What?
- Why?
- Unanswered questions

What?



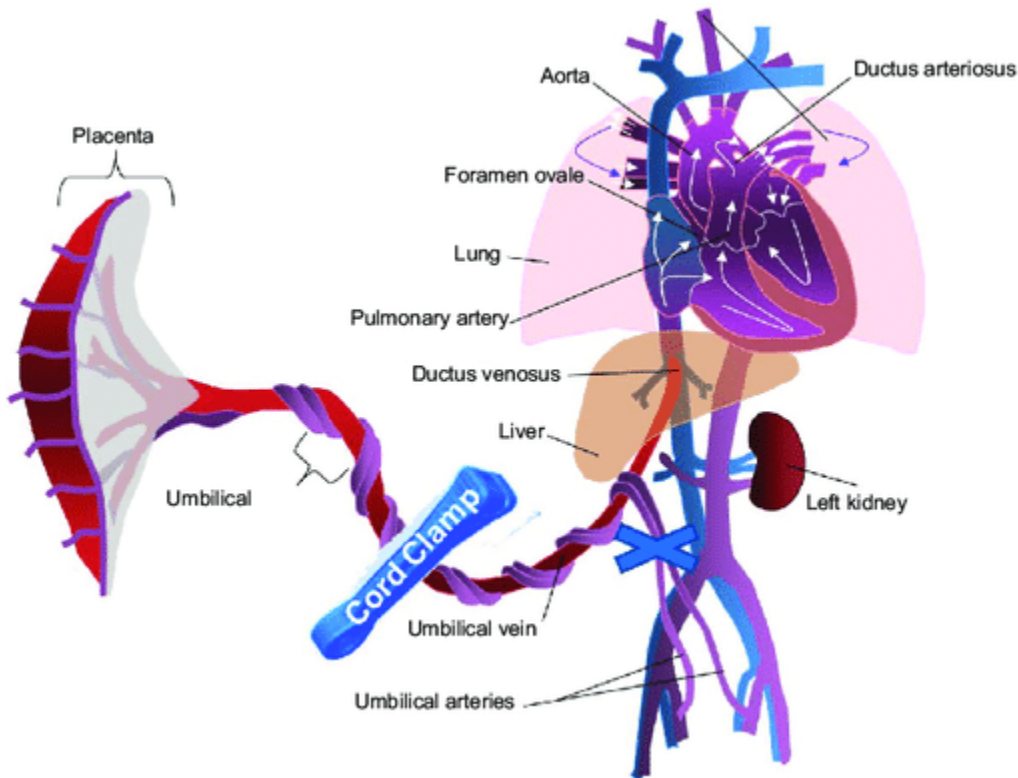
- Defined as delayed clamping of umbilical cord beyond 30 seconds

Table 1. Current recommendations on umbilical cord clamping from professional organizations.

Organization	Year	Recommendation
World Health Organization (WHO) [6,7]	2006, most recently updated 2017	“In newly-born term or preterm babies who do not require positive-pressure ventilation, the cord should not be clamped earlier than one minute after birth.” “Delayed umbilical cord clamping (not earlier than 1 min after birth) is recommended for improved maternal and infant health and nutrition outcomes.”
International Liaison Committee on Resuscitation (ILCOR) [8]	2010, updated 2015	“DCC for longer than 30 s is reasonable for both term and preterm infants who do not require resuscitation at birth”
Neonatal Resuscitation Program (NRP) guidelines from the American Academy of Pediatrics (AAP) [9]	2017	“Delay in umbilical cord clamping for at least 30–60 s for most vigorous term and preterm infants.”
American College of Obstetricians and Gynecologists (ACOG) [10]	2010, recently updated in 2017	“Delay in umbilical cord clamping in vigorous term and preterm infants for at least 30–60 s after birth”
National Institute for Health and Care Excellence (United Kingdom) [11,12]	2014, updated 2017	“Do not clamp the cord earlier than 1 min from the birth of the baby unless there is concern about the integrity of the cord or the baby has a heart rate below 60 beats/minute that is not getting faster.”
American College of Nurse–Midwives [13]	2014	“For term newborns, delaying the clamping of the cord for 5 min if the newborn is placed skin-to-skin or 2 min with the newborn at or below the level of the introitus ensures the greatest benefit. For preterm newborns, the benefits of delaying cord clamping for 30 to 60 s include a significant reduction in intraventricular hemorrhage and a reduced need for blood transfusion.”
Society of Obstetricians and Gynecologists of Canada [14]	2009, reaffirmed 2018	“Whenever possible, delaying cord clamping by at least 60 s is preferred to clamping earlier in premature newborns (<37 weeks’ gestation) since there is less intraventricular hemorrhage and less need for transfusion in those with late clamping.”

DCC, delayed cord clamping.

Why?



Clamping cord immediately:

Reduces preload to the heart by blocking 40% of venous return from the placenta via the umbilical vein

Increases afterload dramatically by obstructing the umbilical arteries thus increasing peripheral vascular resistance

= **Reduced cardiac output**

Why



- Physiologically logical
- Evidence?
 - Recent systematic review and meta-analysis
 - American journal of Obstetrics and Gynecology 2018
 - 27 studies 2800 infants
 - APTS (Australian placental transfusion study) NEJM 2017 1600 infants
 - Cochrane review 2012

TABLE 2

Meta-analyses of delayed vs early cord clamping in preterm infants born <37 weeks' gestation and extremely preterm infants born ≤28 weeks' gestation

Outcome	Studies/ participants	Effect estimate: RR [95% CI]; heterogeneity I ²	RD [95% CI]; weighted mean % of events in early vs delayed group
All infants born <37 wk			
Hospital mortality	18/2834	0.68 [0.52–0.90]	–0.03 [–0.05 to –0.01]; 8% vs 5%
Maternal postpartum hemorrhage (>500 mL)	4/634	0.94 [0.72–1.23]	
Maternal blood transfusion	3/1906	0.84 [0.50–1.39]	
Apgar score <4 at 1 min	2/1600	0.82 [0.67–1.00]	
Apgar score <8 at 5 min	3/1683	1.03 [0.91–1.17]	
Cardiorespiratory support at resuscitation	10/748	0.89 [0.71–1.11]	
Intubation in delivery room	6/532	0.96 [0.82–1.13]	
Temperature on admission, °C	11/2317	MD –0.02 [–0.07 to 0.03]; 50%	
Severe intraventricular hemorrhage	11/2300	0.87 [0.59–1.27]	
Intraventricular hemorrhage—any	19/2871	0.87 [0.75–1.00]	–0.03 [–0.06 to 0.00]; 13% vs 10%
Periventricular leukomalacia	8/1977	0.71 [0.39–1.27]	
Combined periventricular leukomalacia or porencephaly or echodense intraparenchymal lesions or ventriculomegaly	6/1920	0.77 [0.56–1.06]	
Mechanical ventilation	9/686	0.95 [0.84–1.07]	
Chronic lung disease ≥36 wk	7/1951	1.02 [0.93–1.12]	
Patent ductus arteriosus	12/2397	0.96 [0.84–1.09]	
Necrotizing enterocolitis	12/2397	0.88 [0.65–1.18]	
Late-onset sepsis	10/2146	0.95 [0.80–1.13]; 19%	
Severe retinopathy of prematurity	5/1893	0.74 [0.51–1.07]	
Peak hematocrit, %	2/1587	MD 2.73 [1.94–3.52]	
Blood transfusion	13/2595	0.81 [0.74–0.87]; 61%	–0.10 [–0.13 to –0.06]; 50% vs 40%
Polycythemia (hematocrit >65%)	13/2529	2.65 [1.61–4.37]	
Partial exchange transfusion	4/1743	0.14 [0.01–2.74]	
Peak bilirubin, μmol/L	15/2358	MD 4.43 [1.15–7.71]; 77%	
Exchange transfusion	7/2139	0.29 [0.05–1.73]	



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For infants <28/40



Infants born ≤ 28 wk gestation

Hospital mortality	3/996	0.70 [0.51–0.95]	–0.05 [–0.09 to –0.01]: 17% vs 12%
Severe intraventricular hemorrhage	3/967	0.80 [0.51–1.25]	
Chronic lung disease ≥ 36 wk	3/869	0.99 [0.91–1.09]	
Necrotizing enterocolitis	4/977	0.87 [0.61–1.24]	
Late-onset sepsis	3/925	1.07 [0.87–1.31]	
Severe retinopathy of prematurity	2/839	0.72 [0.47–1.09]	
Blood transfusion	2/941	0.91 [0.85–0.97]: 39%	–0.07 [–0.13 to –0.02]: 82% vs 75%

Benefits



Why?-cardiovascular



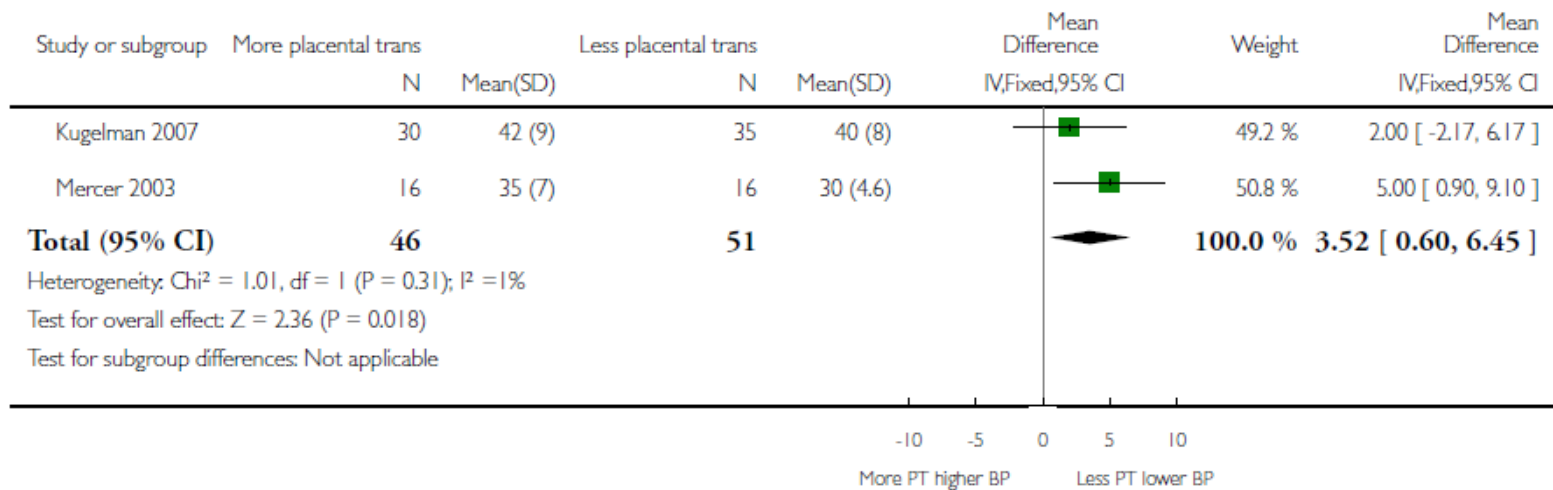
- 30% increase in blood volume
- More stable cardiac output
- Fewer blood transfusions
 - NNT 10
- Increased ferritin stores at 4 months
- Inotropes
 - Significantly less need (RR 0.42) (in Cochrane 2012)

Analysis 1.16. Comparison 1 More placental transfusion (delayed clamping) versus less placental transfusion (early clamping), Outcome 16 Mean arterial blood pressure after birth.

Review: Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes

Comparison: 1 More placental transfusion (delayed clamping) versus less placental transfusion (early clamping)

Outcome: 16 Mean arterial blood pressure after birth

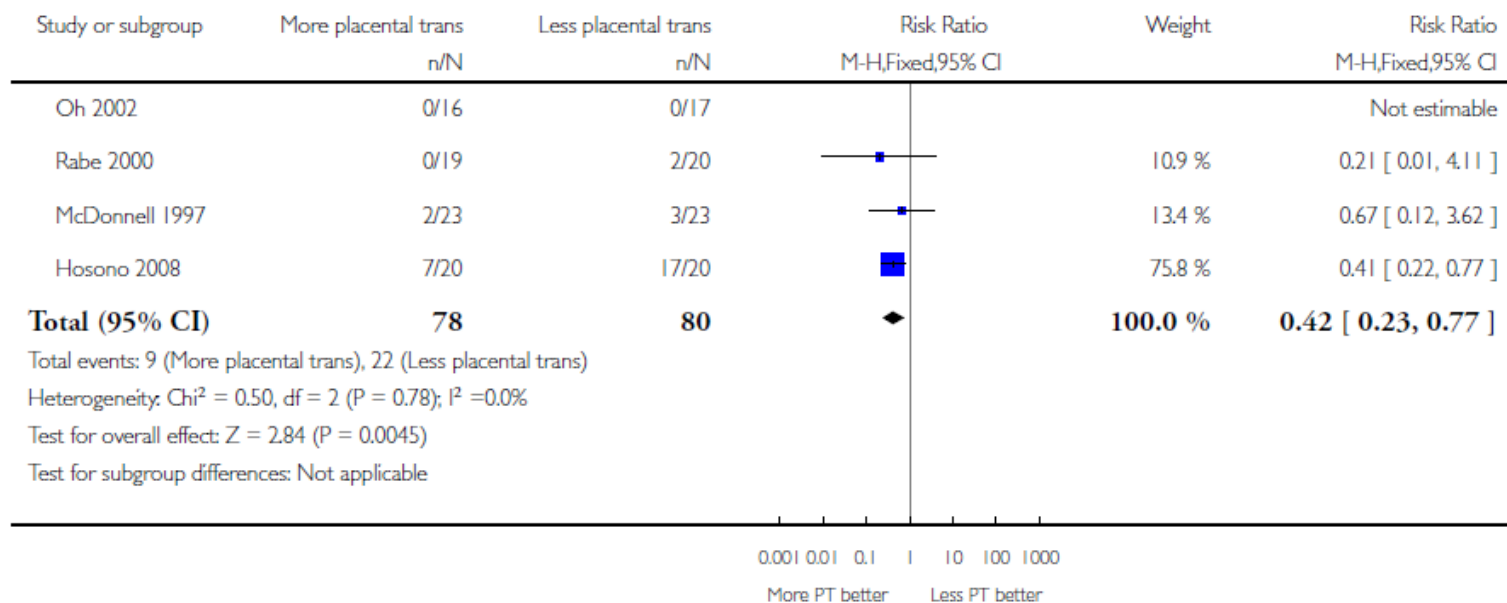


Analysis 1.19. Comparison 1 More placental transfusion (delayed clamping) versus less placental transfusion (early clamping), Outcome 19 Inotropics for low blood pressure.

Review: Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes

Comparison: 1 More placental transfusion (delayed clamping) versus less placental transfusion (early clamping)

Outcome: 19 Inotropics for low blood pressure



Neuro



- Fewer IVHs (all grades, Cochrane 2012)
 - RR 0.59
 - No difference in grade 3/4 IVH
 - Not seen in more recent meta-analysis (2018)
- Increased myelination
 - Reduction seen in autism
- Improved ferritin stores
 - Correlate with increased cognitive, social, emotional and behavioural developmental outcomes
- No large long term studies as yet

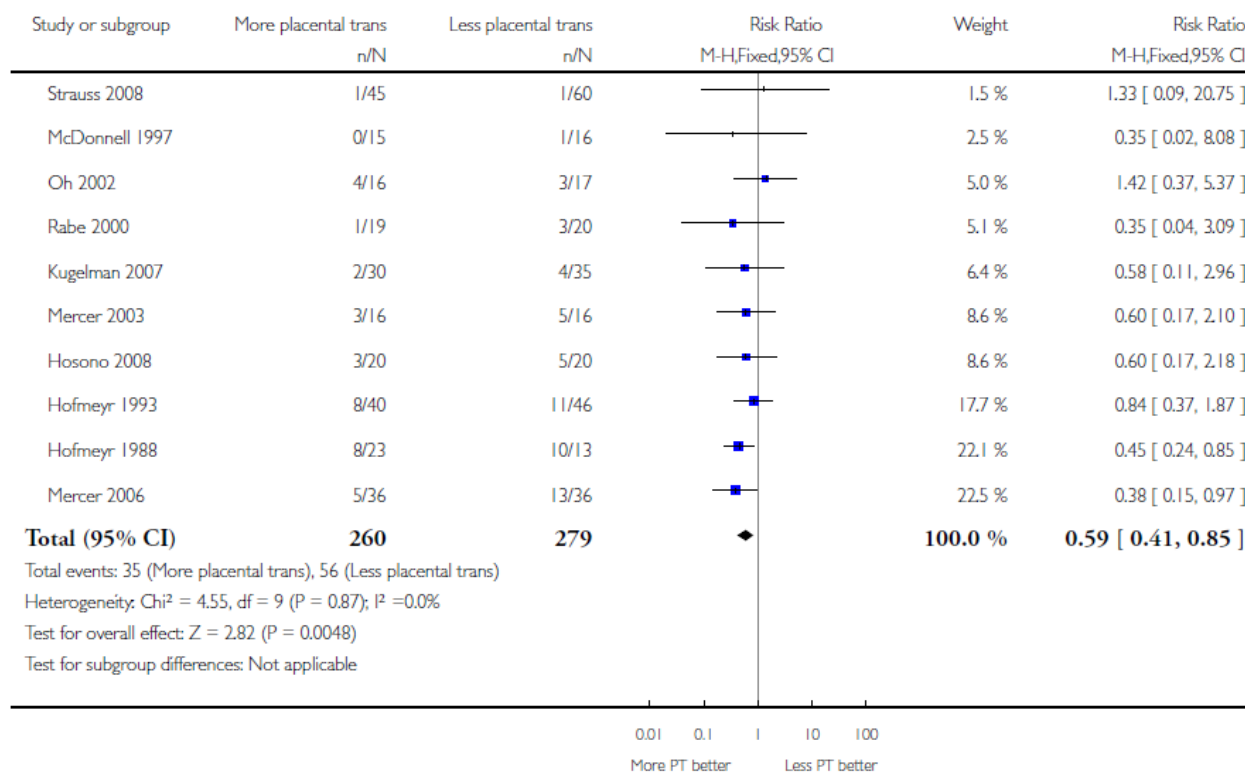


Analysis 1.21. Comparison 1 More placental transfusion (delayed clamping) versus less placental transfusion (early clamping), Outcome 21 Intraventricular haemorrhage (all grades).

Review: Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes

Comparison: 1 More placental transfusion (delayed clamping) versus less placental transfusion (early clamping)

Outcome: 21 Intraventricular haemorrhage (all grades)



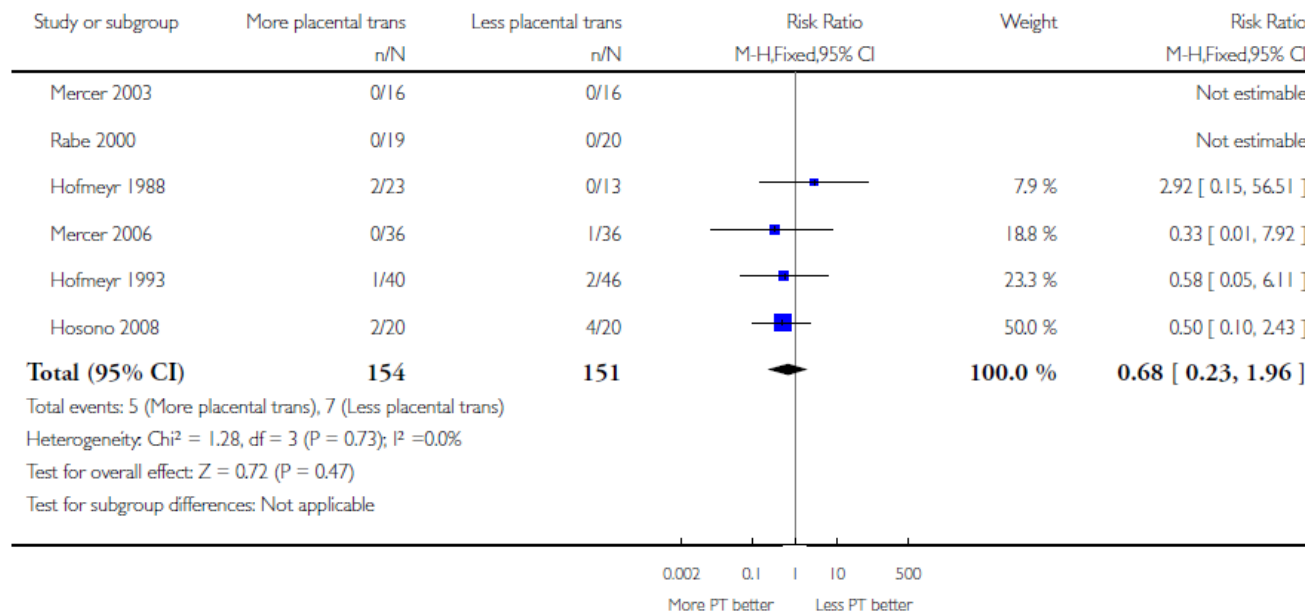


Analysis 1.2. Comparison 1 More placental transfusion (delayed clamping) versus less placental transfusion (early clamping), Outcome 2 Severe intraventricular haemorrhage.

Review: Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes

Comparison: 1 More placental transfusion (delayed clamping) versus less placental transfusion (early clamping)

Outcome: 2 Severe intraventricular haemorrhage



GI



- Less NEC
 - Meta-analysis 6 studies, 296 infants
 - 12% NEC v 20.6%
 - NNT 12
- 2018 meta-analysis
 - no difference (4 studies, 977 participants)

Infection



- Less late onset sepsis?
- Increased immunoglobulin
- More anti-oxidant capacity

Mortality



- 2018 meta-analysis
- RR 0.68
- NNT 33

Why mortality difference?



- Increased red cell mass-increased oxygen carrying capacity without increased FiO_2
- Increased stem cells- reduced inflammatory cascade
- Maintained cardiac output
- Avoided unnecessary intervention
 - Most infants breathing by 60s

But



- More jaundice
 - But not exchange transfusions
- More polycythaemia
 - But not dilutional exchange transfusions
- ?thermoregulatory challenge
 - No difference in admission temperature in APTS

For mother



- No increase in postpartum haemorrhage
- No increase in blood transfusions

Unanswered questions

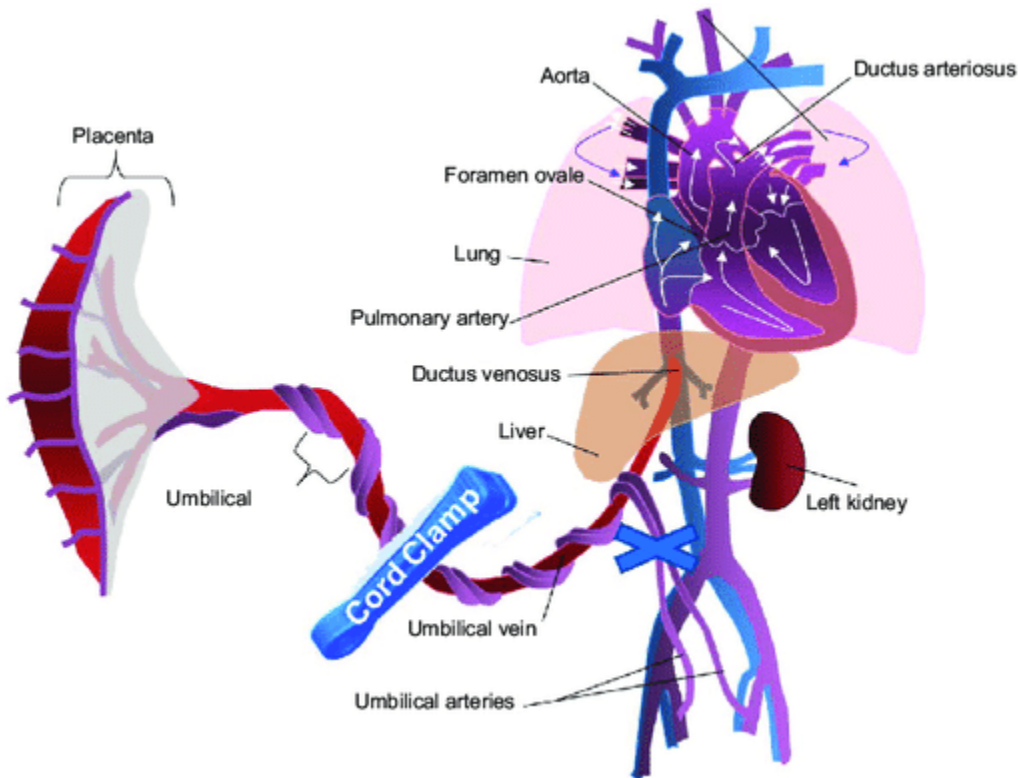


What about resuscitation “on the cord”?



- Good theoretical benefit
- Inflating lungs-increase LV preload-stabilise cardiac output

Why?



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What about resuscitation “on the cord”?



- Good theoretical benefit
- Inflating lungs-increase LV preload-stabilise cardiac output
- 1 RCT of DCC +/-respiratory support
- 150 infants <32/40
- No significant differences

- BUT
 - 90% established regular respirations before 60s

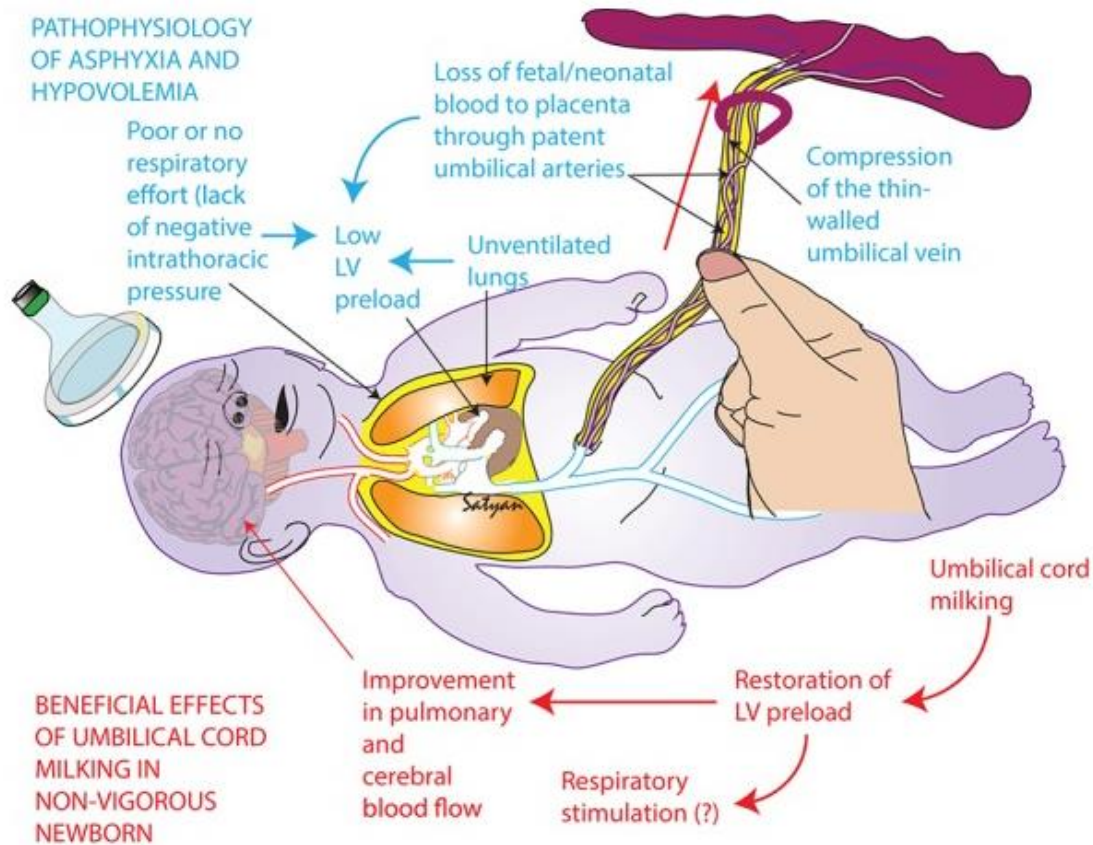
What about umbilical cord milking?



- 20s of cord stripping x4
- Takes 6s
- Should allow for cord clamping and then resuscitation

- Animal studies
 - Increased carotid artery pressure
 - Theoretical risk of IVH

Why?



Beneficial effects of umbilical cord milking in non-vigorous newborns (Satyan Lakshminrusimha, UC Davis, copyright).

UCM



- Infants >35/40
 - Increased Hb and iron stores at 6/52
 - Increased jaundice
- Infants <32/40, 531 infants, RCT v **ICC**
 - Reduced mortality, NEC and infection
- Infants 23-34/40, 282 infants
 - DCC v UCM
 - No difference in Hb, jaundice, NEC, IVH
 - But only 29 infants 23-28/40

Conclusion-DCC



- NNT 38 to reduce neonatal mortality
- NNT 12 to reduce NEC
- Fewer blood transfusions (NNT 10)
- Lower inotrope requirement
- Possible reduction in IVH

- Delayed cord clamping very cheap intervention



- UCM probably safe
- Maybe alternative to ICC if infant needs resuscitation
- Resuscitation on cord
 - More research needed
 - Will need very close working with maternity!

Any questions?





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