5 Should routine controlled cord traction be part of the active management of third stage of labor? The Tracor multicenter randomized controlled trial

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OBJECTIVE: Active management of the third stage of labor is recommended for preventing postpartum hemorrhage (PPH). However, the specific effects of each of its components have not been adequately evaluated. The TRACOR Study aimed to assess the impact of controlled cord traction on the incidence of PPH and other characteristics of the third stage of labor, in a high-resource setting.

STUDY DESIGN: Randomized controlled trial conducted between 01/2010 and 01/2011 in 5 French university hospitals. 4058 women aged ≥18, with a planned vaginal delivery, at a gestational age ≥35 weeks, with a singleton fetus were randomly assigned to have third stage of labor managed either by controlled cord traction (CCT) or by standard placenta expulsion (SPE) i.e. awaiting the spontaneous placental separation before facilitating its expulsion. Prophylactic oxytocin just after birth was administered in the 2 arms. The primary outcome was the incidence of PPH ≥500 mL as measured in a collector bag.

RESULTS: The incidence of PPH was not different in the CCT (9.8% (196/2005) and in the SPE (10.3% (206/2008) groups, RR 0.95, 95% CI (0.79 to 1.15). The need for manual removal of placenta was significantly less frequent in the CCT than in the SPE group (4.2%(85/2033) and 6.1%(123/2024), RR 0.69, 95%CI (0.53 to 0.90)); as was third stage > 15 min (4.5% (91/2030) and 14.3% (289/2020), RR 0.31, 95%CI 0.25 to 0.39)). Women in the CCT group reported a significantly lower intensity of pain and discomfort during the third stage than those in the SPE group. No uterine inversion occurred in either arm.

CONCLUSION: Controlled cord traction does not decrease the incidence of PPH. However, in hospital settings where deliveries are managed by trained clinicians, the benefit/harm balance of controlled cord traction is in favor of its integration in routine practice as it is safe and results in shorter duration of third stage, less need for manual removal of placenta, and higher satisfaction of women.

Main outcomes

	Controlled Cord Traction	Standard Placenta Expulsion	Risk ratio (95% CI)	Mean difference (95% CI)
Blood loss ≥ 500mL	196/2005 (9.8)	206/2008 (10.3)	0.95 (0.79-1.15)	/
Total blood loss (mL) (mean (SD) (n))	207.3 (5.1) (2005)	216.7 (6.0) (2008)	/	-9.4 (-24.8;6.0)
Blood transfusion for PPH	12/2034 (0.6)	9/2024 (0.4)	1.33 (0.56-3.14)	/
Arterial embolization/surgery for PPH	3/2034 (0.1)	5/2024 (0.3)	0.60 (0.14-2.49)	/
Peripartum change in Hb*(g/dL) (mean (SD) (n))	0.86 (0.03) (1961)	0.87 (0.03) (1953)	/	-0.02 (-0.10;0.07)
Peripartum change in Ht* (%) (mean (SD) (n))	2.14 (0.09) (1904)	2.19 (0.09) (1890)	/	-0.05 (-0.29;0.19)
Duration of third stage (min) (mean (SD) (n))	5.46 (0.11) (2030)	8.72 (0.15) (2020)	/	-3.26 (-3.62; -2.90)
Third stage ≥ 15 min	91/2030 (4.5)	289/2020 (14.3)	0.31 (0.25-0.39)	/
Manual removal of placenta	85/2033 (4.2)	123/2024 (6.1)	0.69 (0.53-0.90)	/
Additional uterotonics after placenta delivery	727/2030 (35.8)	805/2024 (39.8)	0.92 (0.83-0.97)	/
Maternal pain during 3rd stage	109/1892 (5.8)	138/1868 (7.4)	0.78 (0.61-0.99)	/
Cord rupture	89/2034 (4.4)	2/2024 (0.1)	44.3 (10.9-179.6)	/

Data are n/N (%) unless otherwise stated.

* Prepartum Hb and Ht measured within 8th month of gestation and arrival in labor ward; postpartum Hb and Ht measured at Day 2 postpartum.

6 Cervical funneling or intraamniotic debris and preterm birth in nulliparous women with short cervix

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OBJECTIVE: To evaluate whether the presence of cervical funneling or intra-amniotic debris is associated with higher rates of preterm birth (PTB) in asymptomatic nulliparous women with a short cervical length (CL).

STUDY DESIGN: Secondary analysis of a multicenter trial of women between 16 and 22 weeks with a singleton gestation and a CL <30 mm on transvaginal ultrasound randomized to either 17 hydroxyprogesterone caproate (17-OHPc) or placebo. Sonographers were centrally certified in CL measurement, as well as identification of intra-amniotic debris and cervical funneling (with measurement of the funnel if present). Univariable and multivariable analyses were performed.

RESULTS: Of the 657 randomized patients, 157 (24%) had funneling, 78 (12%) had debris, and 45 (7%) had both on the screening ultrasound. Women with either of these findings were older (22.7 vs. 22.0 mean years, p=0.03), had a higher pre-pregnancy body mass index (27.6 vs. 25.0 kg/m2, p<0.001) and a lower CL (19.5 vs. 25.6 mm, p<0.001) than those without these findings. PTB < 37 wks was higher for women with a funnel (2.2 OR, 95% CI 1.5-3.3) or debris (1.7 OR, 95% CI 1.0-2.9). Results were similar for progressively earlier preterm delivery (Table). The associations persisted when controlling for 17-OHPc administration, but not after adjusting for CL, except in the case of debris and delivery prior to 35, 34, or 32 weeks. Preterm birth was also associated with the length of the funnel, but was no longer significant after controlling for CL.

CONCLUSION: The presence of cervical funneling is not independently associated with preterm birth in nulliparous women with a short cervix. However, the presence of intra-amniotic debris increases the risk of early preterm birth (<35 wk) independently of the cervical length.

Outcome	Univariable OR (95% CI)	Multivariable OR (95% CI)
Funnel		
PTB <37 wks	2.2 (1.5-3.3)	1.1 (0.7-1.8)
PTB <35 wks	2.8 (1.8-4.4)	1.3 (0.7-2.4)
PTB <34 wks	2.8 (1.8-4.5)	1.4 (0.8-2.5)
PTB <32 wks	3.7 (2.1-6.4)	1.6 (0.8-3.2)
Debris		
PTB <37 wks	1.7 (1.0-2.9)	1.1 (0.6-1.9)
PTB <35 wks	3.1 (1.8-5.2)	1.9 (1.0-3.4)
PTB <34 wks	3.3 (1.9-5.6)	2.0 (1.1-3.7)
PTB <32 wks	5.1 (2.8-9.2)	3.1 (1.6-5.9)

7 The Twin Birth Study: a multicenter RCT of planned cesarean section (CS) and planned vaginal birth (VB) for twin pregnancies 320 to 386/7 weeks

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OBJECTIVE: To compare planned CS with planned VB for twins 320/7 to 386/7 weeks, if the first twin is cephalic.

STUDY DESIGN: Prospective RCT. Eligibility: Twins 32 to 38+6weeks, live fetuses, Twin A cephalic, EFW 1500g- 4000g. Exclusion: Fetal

reduction at >13 wks gestation, lethal fetal anomaly, contraindication to labour. Delivery planned between 375/7 to 386/7 weeks by CS or inducing labour. Primary composite outcome: perinatal/neonatal mortality and/or serious neonatal morbidity. 2800 patients required to detect reduction of primary outcome from 4% to 2%. power 80%, 2-sided, α error of 0.05. A logistic model was used with generalized estimating equations to account for correlation between babies from the same pregnancy.

RESULTS: 2804 women randomized from 26 countries. 1398 to planned CS vs.1406 to planned VB. There was no significant difference between treatment groups. Fifty seven babies of 2781(2.05%) experienced the primary outcome in planned CS vs.52 of 2782 (1.87%) in planned VB (OR1.098,CI 0.726 -1.663,p = 0.6569). There was no significant interaction between treatment group and parity, GA at randomization, mother's age, presentation of twin B, Chorionicity, and country's PNMR.Twin B more likely to experience the primary outcome (OR=1.895,CI:1.329-2.703, p=0.0003). The interaction between treatment group and birth order was not significant (OR;A=1.239; OR;B=1.030, p=0.6125). 89 9% of the women who planned CS delivered both babies by CS. 60.45% in planned VB delivered at least twin A vaginally. 4% of women in planned VB group delivered twin B by CS following VB of twin A. Women in the planned CS delivered earlier but had no increase in maternal mortality or morbidity compared to planned VB.

CONCLUSION: Planned CS in twins at 32-38 week does not decrease (or increase) perinatal/neonatal death or serious neonatal morbidity vs planned VB when the first twin is cephalic.

8 Whole metagenomic shotgun sequencing reveals a vibrant placental microbiome harboring metabolic function

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OBJECTIVE: Humans and our microbiota have co-evolved as a metabolic and antigenic commune ("microbiome") with a collective genome ("metagenome") which retains body site-specific niches. To date, the human placental microbiome has yet to be robustly interrogated. Since the placenta harbors diverse metabolic and immune regulatory functions, it is unlikely to be "sterile" and is likely a uniqe microbiome niche. Our aim was to leverage our developed Human Microbiome Project pipelines to identify community membership (placental microbiome) and function (metagenomic carriage of metabolic pathways).

STUDY DESIGN: In a strictly matched-cohort design, placentas (n 12) were rigorously sterile collected from term gravidae and stratified by presence or absence of remote antenatal infection (e.g., uncomplicated UTI). Genomic DNA was extracted (MoBIO), and metagenomic libraries were subjected to shotgun sequencing (WGS; Illumina). Host (human) DNA was filter binned, and microbial DNA was analyzed with MG_RAST (taxonomic abundance) and HuMAaN (metabolic pathway reconstruction).

RESULTS: >200 million reads (>36 gigabytes) of WGS data were generated, and 357 megabytes of binned microbial data was analyzed. In total, the placental microbiome comprised of 728 species (from among 329 genus). From the 65 most abundant genus, robust metabolic reconstruction revealed 2413 encoded prokaryotic genes. Antental infection signficatnly increased abundance, diversity, and richness of genus (LDA effect size>4, A), resulting in distinct functional metabolic pathways (B,C). The placental microbiome was not significantly structured by maternal BMI> 30 nor mode of delivery.

CONCLUSION: Metagenomic sequencing reveals for the first time that there exists a vibrant and functional placental microbiome community which is structured by a remote history of maternal antenatal infection. We speculate that the placental microbiome likely contributes to both its metabolic and immune functions, and is essential to human reproduction.

Metagenomics of the human placental microbiome