Delayed cord clamping and acute twin-to-twin transfusion syndrome in vaginally born monochorionic twins: a single-centre retrospective cohort study

Rondagh, M.; Steggerda, S.J.; Vos, M.S. de; Hooper, S.B.; Crossley, K.J.; Akker, T. van den; ... ; Lopriore, E.

Delayed cord clamping and acute twin-to-twin transfusion syndrome in vaginally born monochorionic twins: a single-centre retrospective cohort study

Mathies Rondagh ,[1] Sylke J Steggerda,[2] Marit S de Vos,[3] Stuart B Hooper,[4,5] Kelly J Crossley,[4,6] Thomas van den Akker,[3] L S de Vries,[1] Sophie G Groene ,[7] Femke Slaghekke,[3] Arjan B te Pas,[7] Enrico Lopriore [7]

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/archdischild-2025-329451).

[1]Department of Pediatrics, Leiden University Medical Center, Leiden, ZH, The Netherlands
[2]Leiden University Medical Center, Leiden, ZH, The Netherlands
[3]Department of Obstetrics, Leiden University Medical Center, Leiden, The Netherlands
[4]The Ritchie Centre, Hudson Institute of Medical Research, Clayton, Victoria, Australia
[5]Obstetrics and Gynaecology, Monash University, Melbourne, Victoria, Australia
[6]Department of Obstetrics and Gynaecology, Monash University, Melbourne, Victoria, Australia
[7]Neonatology, Leiden University Medical Center, Leiden, ZH, The Netherlands

Correspondence to
Mathies Rondagh;
m.rondagh@lumc.nl

Received 25 July 2025
Accepted 29 October 2025

To cite: Rondagh M, Steggerda SJ, de Vos MS, *et al*. *Arch Dis Child Fetal Neonatal Ed* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/archdischild-2025-329451

ABSTRACT

Objective To evaluate the prevalence of acute peripartum twin-to-twin transfusion syndrome (TTTS) in vaginally born monochorionic (MC) twin pregnancies, comparing early cord clamping (ECC) to delayed cord clamping (DCC).

Design, setting and patients Single-centre retrospective cohort study including vaginally born MC twins at our institution between January 2020 and April 2025. Acute peripartum TTTS was defined as intertwin haemoglobin (Hb) difference >8 g/dL within 12 hours after birth, without signs of chronic TTTS or twin anaemia polycythaemia sequence. Twins were categorised to the ECC and DCC group if cord clamping occurred ≤60 s or >60 s after birth of the first twin, respectively.

Results Thirty-five twin pregnancies were included (n=17 in the ECC group; n=18 in the DCC group). Acute peripartum TTTS occurred in 0% (0/17) in the ECC group compared with 17% (3/18) in the DCC group (p<0.01). In the ECC group, no cases of severe brain injury were observed, whereas 8% (3/36) of infants in the DCC group, all with acute peripartum TTTS, showed severe brain injury (p<0.01). DCC time of the first born infant was associated with larger intertwin Hb difference (β=0.01, p=0.04). Potential risk factors for acute TTTS included interval between birth and cord clamping of the first infant (OR 1.02, 95% CI 1.00 to 1.03, p<0.03) and total combined diameter of bidirectional placental anastomoses (OR 1.34, 95% CI 0.97 to 1.84, p=0.07).

Conclusion DCC in MC twin pregnancies may be associated with a higher prevalence of acute peripartum TTTS and severe brain injury and is therefore not recommended.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Delayed cord clamping (DCC, >60 s) reduces morbidity and mortality in preterm infants, but its safety in monochorionic (MC) twins regarding the risk of acute peripartum twin-to-twin transfusion syndrome (TTTS) in vaginal births is uncertain.

WHAT THIS STUDY ADDS

⇒ This study shows that DCC in vaginally born untreated MC twins may be associated with an increased risk of acute peripartum TTTS and severe brain injury compared to early cord clamping (≤60 s).

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study highlights potential risks of DCC in MC twin pregnancies, underscoring the need for caution, individualised clinical decision-making and international collaboration to strengthen evidence-based recommendations. Research using animal models may help elucidate the impact of DCC on inter-twin transfusion in MC twins.

INTRODUCTION

Twin-to-twin transfusion syndrome (TTTS) is a known complication in monochorionic (MC) twin pregnancies, resulting from unbalanced blood flow through placental vascular anastomoses.[1] While chronic TTTS is well-characterised and leads to oligohydramnios in the donor and polyhydramnion in the recipient, acute peripartum TTTS is a rare event that occurs suddenly during birth and is reported to occur in <5% of MC twins.[1 2] Acute peripartum TTTS is defined by a rapid, peripartum transfusion of blood from one twin (donor) to the other (recipient), resulting in a significant haemoglobin (Hb) difference (>8 g/dL) and potentially leading to haemodynamic instability in one or both twins.[2] The pathophysiology of acute peripartum TTTS is not well understood and is thought to occur through bidirectional arterio-arterial (AA) or veno-venous (VV) placental anastomoses.[3–5] Delayed cord clamping (DCC, >60 s) has been widely adopted in perinatal practice due to the clear benefits compared to early cord clamping (ECC, ≤60 seconds), including increased survival and decreased morbidity and fewer blood transfusions.[6 7] However, in MC twins, DCC may carry a risk of acute peripartum TTTS, as the shared placental circulation may facilitate intertwin blood transfusion and lead to acute exsanguination.[8–10] Since evidence to support this association is lacking, we performed this study to evaluate the prevalence and risk factors of acute peripartum TTTS in vaginally born MC twins, comparing ECC with DCC.

METHODS

Study design, setting and participants

This single-centre, retrospective, observational cohort study was conducted at the obstetric department and neonatal intensive care unit, Leiden University Medical Center (LUMC, Leiden, The Netherlands). The institutional review board stated that this study did not apply to the Medical Research Involving Human Subjects Act (reference number 25–3006) and informed consent was deemed unnecessary, unless the parents had specifically objected to the use of data for research purposes. The study included all MC twins that were vaginally born at the LUMC between January 2020 and April 2025, with a gestational age (GA) at birth ≥24 weeks. We excluded pregnancies with chronic TTTS, twin anaemia-polycythaemia sequence (TAPS), single or double fetal demise, higher-order multiple pregnancies, congenital anomalies or incomplete data regarding the time of cord clamping or missing Hb levels within 12 hours after birth. Diagnosis of chronic TTTS was based according to standardised antenatal ultrasound criteria.[1] TAPS diagnosis was based on the criteria from Tollenaar *et al*.[11]

We recorded the time from birth to cord clamping for both the first and second twin. Twin pregnancies in this study were classified in the ECC group if the time from birth to cord clamping for the first-born twin was ≤60 s and in the DCC group if the time was >60 s. The DCC group included pregnancies in which either DCC (timing based on the infant's clinical condition) or physiological-based cord clamping (PBCC) using a purpose-designed trolley (Concord, Concord Neonatal B.V., Leiden, The Netherlands).[12–14] For PBCC, the umbilical cord was clamped (minimum of 3 min and maximum of 10 min) once the infant was considered stabilised, defined as achieving a heart rate >100 bpm and an SpO_2 >85% while receiving <40% supplemental oxygen.[14] Furthermore, we recorded the time interval between birth of the first twin and the active stage of labour of the second twin and compared the medians.

Our primary outcome was acute peripartum TTTS, defined as a maximum intertwin Hb difference of >8 g/dL without signs of chronic TTTS or TAPS within 12 hours after birth. Hb levels and reticulocyte counts were assessed at birth using umbilical cord blood or venous blood within 12 hours after birth when available. To ensure valid assessment of the intertwin Hb difference, only Hb levels obtained within 1 hour of each other and from the same sample type (ie, both umbilical cord blood or both venous blood) were included.

Placental characteristics

Each MC placenta was routinely injected with coloured dye to examine the placental anastomoses. Specific colours were used to mark different vessels, enabling clear observation of anastomosis types.[15 16] Intertwin anastomoses, including AA, VV and arterio-venous anastomoses (AV), were quantified, and the diameter of AA and VV anastomoses was measured.[15] When multiple bidirectional AA or VV anastomoses were identified, the total diameter from each individual measurement was summed. After dye injection, photographs were taken and analysed using Image J V.1.57 (National Institutes of Health, USA).

Perinatal and neonatal characteristics

Perinatal data collected included maternal age at birth; gravidity; parity; GA at birth; 1-, 5- and 10-min Apgar scores; sex; and birth weight. Birth weight discordance was calculated as the difference between the larger and smaller twin's birth weight divided by the larger twin's birth weight, expressed as a percentage. Red blood cell (RBC) transfusion, partial exchange transfusion (PET), volume bolus expansion and the need for inotropic medication during the first postnatal day were recorded.

Neuroimaging findings

Cranial ultrasound scans were routinely performed in all MC infants by an experienced neonatologist within 3 days after birth either following local guidelines or for research purposes, using a Canon Aplio i700 system (Canon Medical Systems B.V., The Netherlands). In preterm infants below 32 weeks, early cranial ultrasound was part of standard screening protocols. If an MRI was performed, it was acquired using a 3.0-T MR system (Achieva, Philips Medical Systems, Best, The Netherlands), with a neonatal head coil and according to previously described scan protocol by van Rondagh *et al*[17] We recorded the presence of severe brain injury, defined as high-grade intraventricular haemorrhage (IVH) (grade 3 and/or any grade with periventricular hemorrhagic infarction, PVHI), acute white matter injury (detected as acute ultrasound changes that evolve into cystic white matter injury on follow-up scans or on early MRI), arterial ischaemic stroke, parenchymal haemorrhage and extensive cerebellar haemorrhage.

Statistical analysis

Independent sample t-tests or Wilcoxon rank tests were used to compare continuous variables and $\chi 2$ or Fisher's exact tests for categorical variables. Potential risk factors for acute peripartum TTTS were studied in a logistic regression analysis. Results of the logistic regression are reported as OR with 95% CI. Linear regression was used to assess the association between first twin cord clamping time and intertwin Hb difference. A p value < 0.05 was considered statistically significant. Analyses were performed using SPSS V.29.0 (IBM, Chicago, IL, USA).

RESULTS

A total of 138 MC twins were vaginally born at our centre between January 2020 and April 2025. After assessment of eligibility, we have included 35 pregnancies (70 infants) in this study (online supplemental figure 1). In total, 17 births were categorised in the ECC group and 18 births in the DCC group. The DCC group included 22% (4/18) of pregnancies in which PBCC was applied. Median cord clamping time in the ECC group of the first and second twin was 60 (IQR 60–60) and 60 (IQR 30–120) seconds, respectively. Median cord clamping time of the first and second infant in the DCC group was 180 (IQR 180–240) and 180 (IQR 120–240) seconds, respectively. Except for a higher proportion of female infants in the DCC group (61%, 22/36, vs 35%, 12/34), maternal, perinatal baseline and placental characteristics were comparable between groups (table 1 and online supplemental table 1).

The first Hb measurement in cord or venous blood obtained directly after birth was available in 94% (33/35) of the pregnancies. Mean intertwin Hb-level difference for the first Hb measurement of the ECC and DCC group was 1.7±1.6 and 2.9±2.8 g/dL (p=0.20, table 2), with twin 1 having a higher Hb level. A second Hb measurement within 12 hours after birth was available in 19/35 (54%) of pregnancies, 11 in the ECC group and eight in the DCC group, with a median time at measurement of 212 min (IQR, 114–560).

Table 1 Baseline characteristics

Characteristics	ECC group (n=34, 17 pregnancies)	DCC group (n=36, 18 pregnancies)	P value
Maternal age	31 (28 to 34)	33 (30 to 34)	0.27
Gravidity	2 (1-3)	2 (1-2)	0.66
Parity	1 (0 to 1)	0 (0 to 1)	0.66
Maternal estimated blood loss (mL)	500 (300 to 700)	435 (300 to 1000)	0.91
Cord clamping time first infant (s)	60 (60 to 60)	180 (180 to 240)	<0.01
Cord clamping time second infant (s)	60 (30 to 120)	180 (120 to 240)	<0.01
Apgar score at 1 min	9 (6-9)	9 (7-9)	0.61
Apgar score at 5 min	10 (8 to 10)	10 (8 to 10)	0.94
Apgar score at 10 min	10 (9 to 10)	10 (9 to 10)	0.81
Female	12 (35)	22 (61)	0.03
GA at birth	35.4 (34.0 to 36.1)	34.5 (33.0 to 36.3)	0.64
birth weight	2293 (1880 to 2625)	2110 (1560 to 2628)	0.41
birth weight discordance	9 (7-18)	16 (4 to 30)	0.14

Continuous data are presented as medians with interquartile ranges and categorical data as numbers (n) and percentages (%).
DCC, delayed cord clamping; ECC, early cord clamping; GA, gestational age.

The intertwin Hb difference from this second measurement was 3.3 ± 2.4 g/dL in the ECC group and 4.6 ± 3.6 g/dL in the DCC group (p=0.4); again, twin 1 is higher than twin 2. Acute peripartum TTTS was observed in 0% (0/17) in the ECC group compared with 17% (3/18) in the DCC group (p<0.01). Notably, in twins that had a cord clamping time >180 s for the first infant, acute TTTS (twin 2 to twin 1) was observed in 43% (3/7). In the PBCC group, 75% (3/4) of the twin pairs showed acute peripartum TTTS. Cord clamping time of the first twin was significantly associated with Hb difference within 12 hours after birth (β=0.01 g/dL per second; R^2 = 0.13; p=0.04, figure 1).

In the acute peripartum TTTS group, two recipients were born first, and one donor was born first (table 3). Median cord clamping time was significantly longer in infants with acute peripartum TTTS (240 s, IQR 210–480) than those without (60 s, IQR 60–180; p<0.01). There was no difference in the median interval between the birth of the first twin and the active stage of labour between the acute peripartum TTTS group (6 m, IQR 2–36 m) and the group without acute TTTS (4 m, IQR 3–6 m, p=0.50). In all MC twin pregnancies with acute peripartum TTTS, one of the co-twins developed severe brain injury (two recipients and one donor, figure 2).

In the ECC group, no cases of acute peripartum TTTS and/or severe brain injury were observed, whereas 8% (3/36) of infants in the DCC group showed acute peripartum TTTS and developed severe brain injury (p<0.01). There were no significant differences between the ECC and DCC group in the number of RBC transfusions, PET, fluid expansions or inotropic support. No mortality was reported in the ECC group, whereas one infant in the DCC group died following redirection of care due to severe brain injury.

In the univariate analysis, a longer interval from birth to cord clamping in the first infant was associated with an increased risk of acute peripartum TTTS (OR 1.02; 95% CI 1.00 to 1.03, p=0.03, online supplemental table 2). Thus, for every one-second increase of the interval between birth and cord clamping, there is a 2% increase in the risk of acute peripartum TTTS. Other factors, including the interval between birth of the first twin and the active stage of labour for the second twin, and the total diameters of AA, VV and all bidirectional anastomoses, were not significantly associated with increased risk. However, a larger total diameter of

Table 2 Hb levels in ECC group and DCC group and acute peripartum TTTS

	Early cord clamping (ECC) group (n=34, 17 pregnancies)	Delayed cord clamping (DCC) group (n=36, 18 pregnancies)	P value	Acute peripartum TTTS (n=6, 3 pregnancies)	Total population* (n=64, 32 pregnancies)	P value
First Hb level in first twin (g/dL)	15.9±1.4	17.6±3.1	0.09	19.2±5.8	16.6±2.1	0.53
First Hb level in second twin (g/dL)	16.5±2.9	16.6±3.1	0.93	15.0±1.5	16.7±3.0	0.40
Inter-twin first Hb difference (g/dL)	1.7±1.6	2.9±2.8	0.20	4.1±5.5	2.2±1.9	0.62
Second Hb level within 12 hours in first twin (g/dL)	16.9±2.9	17.0±4.5	0.71	17.5±7.1	16.8±2.9	0.50
Second Hb level within 12 hours in second twin (g/dL)	18.0±3.5	16.4±3.4	0.36	15.0±4.1	17.8±3.2	0.34
Inter-twin second Hb difference within 12 hours (g/dL)	3.3±2.4	4.6±3.6	0.41	8.6±1.1	2.9±2.2	<0.01
Inter-twin maximum Hb difference within 12 hours (g/dL)	3.2±2.1	3.9±3.3	0.62	9.66±0.7	2.96±2.1	<0.01
Blood transfusion (%)	0 (0)	2 (6)	0.16	2 (33)	0 (0)	<0.001
Partial exchange transfusion (%)	0 (0)	1 (3)	0.33	1 (17)	0 (0)	0.001
Fluid expansion (%)	3 (9)	5 (14)	0.51	3 (50)	5 (8)	0.002

Hb, haemoglobin; TTTS, twin-to-twin transfusion syndrome.

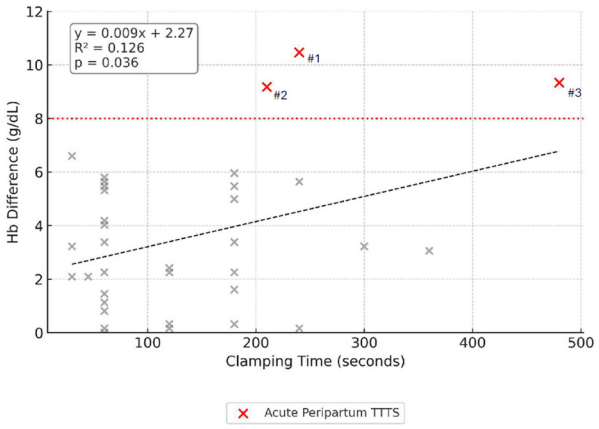

Figure 1 Relationship between clamping time for the first twin and inter-twin haemoglobin difference. This scatterplot shows the relationship between clamping time (seconds) and largest haemoglobin (Hb) difference (g/dL) between donor and recipient within 12 hours after birth. Each grey dot represents a twin pair. Each red cross marks a twin pair diagnosed with acute peripartum twin-to-twin transfusion syndrome (TTTS). The dashed line represents the linear regression trendline with corresponding regression equations, R^2 values and p values. The red dotted line represents the diagnostic threshold for acute peripartum TTTS, defined as an intertwin Hb difference of >8 g/dL. # indicates the case number of each twin.

bidirectional anastomoses showed a trend toward increased risk (OR 1.34; 95% CI 0.97 to 1.84; p=0.07).

DISCUSSION

This study shows an increased risk of acute peripartum TTTS of one in six for MC twin pairs born vaginally with DCC, whereas no cases of acute peripartum TTTS were observed among those with ECC. In the case of acute peripartum TTTS, half of the infants developed severe postnatal brain injury, and none of the affected twin pairs were without brain injury, underscoring the potential serious complications of DCC in MC twin vaginal births. The prevalence of acute peripartum TTTS in the MC pregnancies with DCC observed in this cohort is markedly higher than previously reported in MC pregnancies with ECC. Our study group previously reported a rate of 4.3% in vaginally born MC twin pairs with ECC.[2] Another important finding in our study was that a larger total diameter of bidirectional placental anastomoses showed a trend towards significance, suggesting an increased risk of acute peripartum TTTS in MC pregnancies with large bidirectional anastomoses.

DCC allowed prolonged placental shared circulation, facilitating continued transfusion between the donor and recipient twin and was associated with larger intertwin Hb differences.[8 18–20] This imbalance may lead to acute anaemia and hypovolaemia in the donor and polycythaemia and hypervolaemia in the recipient and potentially contributes to multi-organ failure and severe brain injury.[10 21] Assessment of inter-twin Hb difference solely in cord blood in the immediate postpartum period may underestimate the true extent of inter-twin transfusion as haemodilution in the recipient and haemoconcentration in the donor often occur in minutes to hours following birth, potentially masking early haemodynamic shifts. Haemodilution in the recipient arises as excess blood volume expands the plasma compartment over time, leading to a reduction in Hb concentration. In contrast, haemoconcentration in the donor results from reduced circulating volume and delayed plasma compensation,

Table 3 Characteristics of MC pregnancies with acute peripartum TTTS

Acute TTTS	Twin complication	BWD	MCA-PSV (MoM, GA)	Cardiotocography	GA at birth	BW (g)	Birth order	Time of cord clamping	Treatment	Hb-level after birth	Hb -difference (g/dL)	Neonatal outcome
Donor (#A1)	sFGR (smaller co-twin)	36.6%	54 cm/s, (1.22, 31+6)	Complicated decelerations	32 weeks	1300	Second	4 min	None	16.1	9.5	Survival
Recipient (#B1)	sFGR (larger co-twin)		48 cm/s(1.09, 31+6)	15–30 min before birth of first twin; bradycardia before birth of second twin		2050	First	4 min	PET fluid expansion	25.6		Neonatal death
Donor (#A2)	sFGR (larger co-twin)	25.8%	28.7 cm/s (0.60, 33+4)	Bradycardia of donor twin	34 weeks	2115	First	3 min 30 s	RBC	9.5	10.9	Survival
Recipient (#B2)	sFGR (smaller co-twin)		57.8 cm/s (1.21, 33+4)	(5 min before birth)		1570	Second	1 min 30 s	Fluid expansion	20.4		Severe brain injury
Donor (#A3)	Uncomplicated	4.2%	NR	Uneventful until 30 min	29 weeks	1360	Second	8 min	RBC	10.6	12.6	Severe brain injury
Recipient (#B3)	Uncomplicated		NR	before birth. Last 30 min suboptimal registration		1420	First	7 min	Fluid expansion	23.2		Survival

TTTS, twin-twin transfusion syndrome.BW, birth weight; BWD, birth weight discordance; GA, gestational age; g/dL, grams per deciliter; Hb, haemoglobin; HIE, hypoxic-ischaemic encephalopathy; IVH, intraventricular haemorrhage; MCA-PSV, middle cerebral artery peak systolic velocity; MoM, multiples of the median; NR, not recorded; PET, partial exchange transfusion; PHVI, periventricular haemorrhagic infarction; RBC, red blood cell transfusion; sFGR, selective fetal growth restriction.

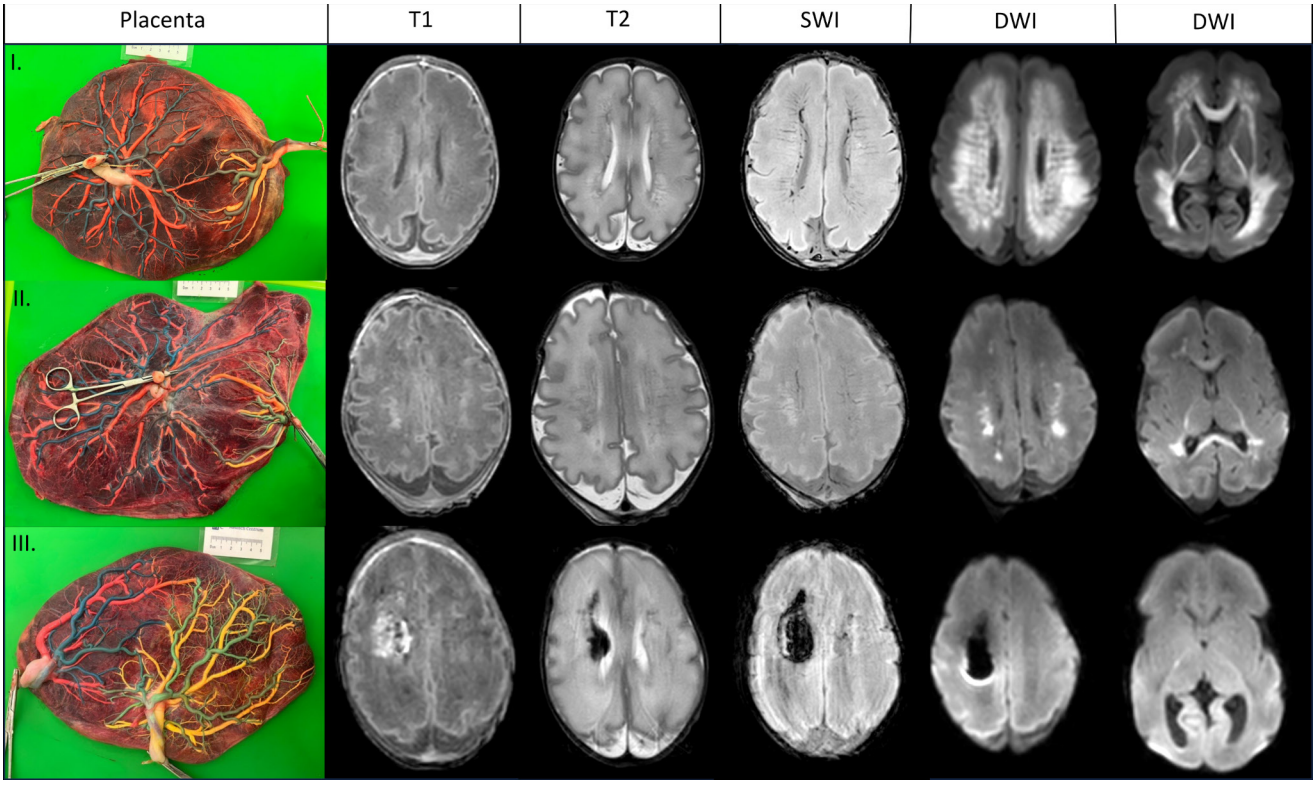

Figure 2 Brain injury pattern of twins after acute peripartum TTTS placental and neonatal MRI findings of the twins with delayed cord clamping and acute peripartum TTTS, including dye-injected placentas and MRI sequences: T1-weighted, T2-weighted, susceptibility-weighted imaging (SWI) and diffusion-weighted imaging (DWI). The first twin pair (#1A/B) was born vaginally at 32 weeks with a birth weight discordance (BWD) of 37%. The recipient (#1B) showed severe polycythaemia (Hb 25.6 g/dL) and the day five MRI revealed acute and extensive hypoxic ischaemic injury with diffusion restriction throughout the supratentorial white matter, corpus callosum, internal and external capsules and thalami, leading to redirection of care. Placental dye-injection revealed one AA (2.2 mm), 10 AV and one VA anastomosis (I). The second twin pair (#2A/B) was born at 34 weeks with a BWD of 26%, the recipient (#2B) was polycythaemic (Hb 20.4 g/dL) and MRI on day 5 showed acute ischaemic periventricular white matter injury on DWI as well as restricted diffusion in the posterior limb of the internal capsule and corpus callosum. The placenta showed one AA (4.5 mm), one VV (5.0 mm), two AV and four VA anastomoses (II). The third twin pair (#3A/B) was born at 29 weeks; the donor (#3A) was anaemic (Hb 10.6 g/dL) and MRI on day 7 showed a right frontal periventricular haemorrhagic infarction with grade 2 IVH (visible from first day after birth on cranial ultrasound). There is very focal diffusion restriction of the ipsilateral posterior limb of the internal capsule. Placental dye-injection showed one AA (3.10 mm), one VV (3.84 mm), seven AV and 15 venous-arterial (VA) anastomoses (III). AV, arterio-venous anastomoses; AA, arterio-arterial; Hb, haemoglobin; TTTS, twin-to-twin transfusion syndrome; VV, veno-venous.

resulting in a relatively increased Hb level. Hb measurement between 3 and 12 hours postpartum is therefore necessary for a more comprehensive and accurate assessment of volume status and the degree of inter-twin transfusion.

The precise pathophysiological mechanisms underlying acute peripartum TTTS following DCC remain poorly understood. Our study and existing case reports show inconsistent patterns in mode of birth, birth order of donor and recipient and cord clamping timing.[2 8 22 23] This suggests a multifactorial cause of acute peripartum TTTS, potentially involving the presence and the total diameter size of bidirectional anastomoses, establishing lung aeration, fetal positioning, uterine tone, placental location, pressure dynamics during labour, umbilical cord characteristics (insertion, length and umbilical coiling index) and timing of cord clamping.[24–28] There is substantial variation in high-income countries with regard to mode of birth in twin pregnancies. It is therefore important to underscore that placental transfusion dynamics (including the risk of acute peripartum TTTS) may differ from twins born vaginally and twins born through caesarean section. The only observational study evaluating the prevalence of acute peripartum TTTS found that it occurred primarily after vaginal birth.[2] Nonetheless, case reports have also described its occurrence following caesarean section.[29] Current evidence does not establish whether caesarean section reduces the risk of acute peripartum TTTS in MC twins.[2] An innovative acute peripartum TTTS twin lamb model, simulated MC placental shared circulation incorporating AA anastomoses, might provide key insights into these pathophysiological mechanisms. The ongoing study aims to identify key factors contributing to acute TTTS, including HR and BP differences, timing of umbilical cord clamping and uterine contractions.[24 30] Although this sheep model involves caesarean section rather than vaginal birth, it allows precise control of umbilical catheterisation, timing of birth and measurement of inter-twin transfusion. While not directly generalisable to vaginal birth, it will provide important physiological insights that approximate key aspects of the clinical scenario.

The use of selective extrauterine placental perfusion has recently been proposed as a novel strategy in a small case series (n=3) of MC twins born by caesarean section with suspected severe anaemia in the donor twin, whereby the donor cord is left unclamped and the recipient's cord clamped immediately.[20] We think that the only subgroup where this approach may be safe and potentially beneficial is in MC twins with TAPS. In TAPS,

the ubiquitous presence of only a few minuscule vascular anastomoses prevents acute intertwin transfusion events.[31] In other subgroups, including TTTS, large anastomoses including bidirectional AA or VV anastomoses may be present. Whether DCC in the donor (and immediate ECC in the recipient) would lead to increased placental transfusion towards the donor remains unclear and requires further investigation.

The 4–8-min interval after birth reflects a PBCC approach, in which cord clamping is deferred until the newborn has achieved clinical stabilisation. This approach was investigated in the multicentre ABC trial, showing feasibility and safety.[12–14] Importantly, in the ABC-3 trial, uncomplicated MC twins were also included. No clear benefits nor risks were identified in this subgroup, but the overall number of MC twins was small to reach meaningful conclusions.[14] The findings of the ABC-3 trial have influenced current practice at our centre, where DCC or PBCC has become increasingly implemented in both preterm and twin births. In our study, three out of four twin pairs who received PBCC developed acute peripartum TTTS, raising concerns about the safety of this approach. We hypothesise that the mechanism underlying the increased risk of acute peripartum TTTS with PBCC involves the development of a pressure gradient following lung aeration in the first-born twin. As pulmonary vascular resistance decreases, a left-to-right shunt develops across the ductus arteriosus and postductal systemic blood pressure drops, potentially enabling blood to flow through low-resistance bidirectional anastomoses from the twin in utero (donor) to the first-born twin (recipient). However, in the three cases of acute peripartum TTTS, only in two out of three twin pairs was the first-born twin the recipient, suggesting that additional mechanisms may be involved. Severe brain injury was predominantly observed in polycythaemic twins, with patterns consistent with hyperviscosity and venous congestion. These findings suggest that polycythaemia may represent a key mechanism of injury in acute peripartum TTTS, alongside the previously described mechanisms of anaemia and hypovolaemic shock.[32] Moreover, two-thirds of twins with acute peripartum TTTS showed selective fetal growth restriction, often characterised by large bidirectional anastomoses (particularly type 3), which may place this subgroup at increased risk.[26 33] DCC with shorter intervals may still offer physiological benefits while minimising the risk of acute peripartum TTTS. Animal studies may help clarify the optimal timing for cord clamping and identify the clinical conditions under which DCC can be safely applied.

As shown in several randomised controlled trials (RCTs) and systematic reviews, DCC in singletons is associated with improved outcomes. However, most studies did not include twins or did not differentiate between dichorionic (DC) and MC twins. In a recent systematic review regarding DCC in twins (defined as cord clamping >30 s), the authors concluded that DCC may decrease the risk of mortality in preterm twins without an impact on major neonatal morbidities.[9] However, the systematic review was based only on five small retrospective studies and most included only DC twins or did not differentiate between DC and MC twins.[9] Only one study also included MC twins, but the group was too small to reach meaningful conclusions.[34] The optimal timing of cord clamping in MC twins, balancing risks and benefits, remains therefore unclear. Across clinical societies, cord clamping guidance specific to MC twins is absent or limited. As summarised by Song *et al*, most organisations recommend DCC in general but give no specific recommendations for MC twins and are predominately based on caesarean births.[10] Well-designed RCTs differentiating between DC and MC twins (and subtypes of MC subgroups) are urgently needed to identify the benefit and risk of DCC in twin pregnancies.

This is the first study to evaluate the effect of DCC and potential risk of acute TTTS in MC pregnancies. An important strength of this study is the comprehensive and systematic evaluation of acute peripartum TTTS in MC twin pregnancies, including a detailed documentation of peripartum management, routine placental dye-injection of placental anastomoses, multiple postnatal Hb measurements and routine neuroimaging to assess potential brain injury. This study has several limitations, including its relatively small sample size, which is an inherent challenge in researching a rare condition of acute peripartum TTTS. The retrospective nature of the study introduces the risk of selection bias, as the decision to perform ECC or DCC may have been influenced by clinical factors at the time of birth. Therefore, our findings should be interpreted with caution and should be validated in larger multicentre retrospective studies.

To conclude, given the high prevalence of acute peripartum TTTS and its associated risk of severe brain injury, DCC should not be recommended in vaginally born MC twins.

Contributors MR and EL conceptualised and designed the study. SJS, MSdV, TvdA, FS, LSdV, SGG and ABtP contributed to data interpretation and manuscript revision. SBH and KJC provided experimental and physiological expertise and critically reviewed the manuscript. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work. MR is the guarantor and accepts full responsibility for the integrity and accuracy of the work.

Funding Funding was received from the European Society for Paediatric Research (ESPR), Leids Universitair Fonds (LUF), Gratama Stichting (2023-10/W233029-2 GSL), StrongBabies (SB-JO-2023-15), Honors College Leids Universitair Medisch Centrum (240426), Janivo Stichting, Gisela Thier Fonds, Raynor Foundation and Vaillant Stichting.

Competing interests None declared.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer-reviewed.

Data availability statement Data are available upon reasonable request. All data relevant to the study are included in the article or uploaded as supplementary information. All data relevant to the study are included in the article or uploaded as supplementary information. Data are available upon reasonable request.

ORCID iDs
Mathies Rondagh https://orcid.org/0009-0002-1715-093X
Sophie G Groene https://orcid.org/0000-0002-8832-045X
Enrico Lopriore https://orcid.org/0000-0002-3513-5066

REFERENCES

1 Quintero RA, Morales WJ, Allen MH, *et al*. Staging of twin-twin transfusion syndrome. *J Perinatol* 1999;19:550–5.
2 Lopriore E, Holtkamp N, Sueters M, *et al*. Acute peripartum twin-twin transfusion syndrome: incidence, risk factors, placental characteristics and neonatal outcome. *J Obstet Gynaecol Res* 2014;40:18–24.
3 de Villiers SF, Slaghekke F, Middeldorp JM, *et al*. Arterio-arterial vascular anastomoses in monochorionic placentas with and without twin-twin transfusion syndrome. *Placenta* 2012;33:652–4.
4 Umur A, van Gemert MJC, Nikkels PGJ, *et al*. Monochorionic twins and twin-twin transfusion syndrome: the protective role of arterio-arterial anastomoses. *Placenta* 2002;23:201–9.
5 Denbow ML, Cox P, Taylor M, *et al*. Placental angioarchitecture in monochorionic twin pregnancies: relationship to fetal growth, fetofetal transfusion syndrome, and pregnancy outcome. *Am J Obstet Gynecol* 2000;182:417–26.

6 Seidler AL, Libesman S, Hunter KE, *et al*. Short, medium, and long deferral of umbilical cord clamping compared with umbilical cord milking and immediate clamping at preterm birth: a systematic review and network meta-analysis with individual participant data. *Lancet* 2023;402:2223–34.
7 Seidler AL, Aberoumand M, Hunter KE, *et al*. Deferred cord clamping, cord milking, and immediate cord clamping at preterm birth: a systematic review and individual participant data meta-analysis. *Lancet* 2023;402:2209–22.
8 Groene SG, Tollenaar LSA, van der Meeren LE, *et al*. Large Hemoglobin Differences at Birth in Monochorionic Twins with a Placental Chorangioma and Delayed Cord Clamping. *Twin Res Hum Genet* 2021;24:281–4.
9 Chartrand L, Barrington KJ, Dodin P, *et al*. Delayed cord clamping in preterm twin infants: a systematic review and meta-analysis. *Am J Obstet Gynecol* 2025;232:271–9.
10 Song D, Jelks A, Narasimhan SR, *et al*. Cord management strategies in multifetal gestational births. *Semin Perinatol* 2023;47:151743.
11 Tollenaar LSA, Lopriore E, Middeldorp JM, *et al*. Improved prediction of twin anemia-polycythemia sequence by delta middle cerebral artery peak systolic velocity: new antenatal classification system. *Ultrasound Obstet Gynecol* 2019;53:788–93.
12 Brouwer E, Knol R, Vernooij ASN, *et al*. Physiological-based cord clamping in preterm infants using a new purpose-built resuscitation table: a feasibility study. *Arch Dis Child Fetal Neonatal Ed* 2019;104:F396–402.
13 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.
14 Knol R, Brouwer E, van den Akker T, *et al*. Physiological versus time based cord clamping in very preterm infants (ABC3): a parallel-group, multicentre, randomised, controlled superiority trial. *Lancet Reg Health Eur* 2025;48:101146.
15 Lopriore E, Slaghekke F, Middeldorp JM, *et al*. Accurate and simple evaluation of vascular anastomoses in monochorionic placenta using colored dye. *J Vis Exp* 2011;2011:e3208.
16 Spekman JA, Slaghekke F, Lopriore E. The invaluable importance of color dye injection of monochorionic twin placentas. *Am J Obstet Gynecol MFM* 2025;7:101700.
17 Rondagh M, Schrama WJJ, de Vries LS, *et al*. Brain State of the Newborn as a Biomarker for Brain Injury in Infants with Hypoxic-Ischemic Encephalopathy. *J Pediatr* 2025;285:114702.
18 Kosińska-Kaczyńska K, Witwicki J, Saletra-Bielińska A, *et al*. Hemoglobin differences in twins are related to the time of cord clamping, not intertwin transfusion - a prospective cohort study. *BMC Pregnancy Childbirth* 2022;22:619.
19 Zhao DP, Verbeek L, Tollenaar LSA, *et al*. Inter-twin hemoglobin difference at birth in uncomplicated monochorionic twins in relation to the size of the placental anastomoses. *Placenta* 2018;74:28–31.
20 Kuehne B, Trieschmann J, Butzer SK, *et al*. Selective Extrauterine Placental Perfusion in Monochorionic Twins Is Feasible-A Case Series. *Children (Basel)* 2024;11:1256.
21 Couck I, Lewi L. The Placenta in Twin-to-Twin Transfusion Syndrome and Twin Anemia Polycythemia Sequence. *Twin Res Hum Genet* 2016;19:184–90.
22 Sherer DM, Sinkin RA, Metlay LA, *et al*. Acute intrapartum twin-twin transfusion. A case report. *J Reprod Med* 1992;37:184–6.
23 Uotila J, Tammela O. Acute intrapartum fetoplacental transfusion in monochorionic twin pregnancy. *Obstet Gynecol* 1999;94:819–21.
24 Hooper SB, Crossley KJ, Zahra VA, *et al*. Effect of body position and ventilation on umbilical artery and venous blood flows during delayed umbilical cord clamping in preterm lambs. *Arch Dis Child Fetal Neonatal Ed* 2017;102:F312–9.
25 McDonald SD, Narvey M, Ehman W, *et al*. Guideline No. 424: Umbilical Cord Management in Preterm and Term Infants. *J Obstet Gynaecol Can* 2022;44:313–22.
26 Groene SG, Openshaw KM, Jansén-Storbacka LR, *et al*. Impact of placental sharing and large bidirectional anastomoses on birthweight discordance in monochorionic twins: a retrospective cohort study in 449 cases. *Am J Obstet Gynecol* 2022;227:755.
27 Stenning FJ, Polglase GR, Te Pas AB, *et al*. Effect of maternal oxytocin on umbilical venous and arterial blood flows during physiological-based cord clamping in preterm lambs. *PLoS One* 2021;16:e0253306.
28 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:F324–8.
29 Suzuki S, Kubota Y. Acute twin-twin transfusion syndrome without labour. *J Obstet Gynaecol* 2019;39:851–2.
30 Polglase GR, Blank DA, Barton SK, *et al*. Physiologically based cord clamping stabilises cardiac output and reduces cerebrovascular injury in asphyxiated near-term lambs. *Arch Dis Child Fetal Neonatal Ed* 2018;103:F530–8.
31 van de Sande MJA, Lopriore E, Lanna M, *et al*. Single fetal demise in twin anemia-polycythemia sequence: perinatal outcome of surviving cotwin. *Ultrasound Obstet Gynecol* 2025;66:51–5.
32 Emery SP, Bahtiyar MO, Moise KJ, *et al*. The North American Fetal Therapy Network Consensus Statement: Management of Complicated Monochorionic Gestations. *Obstet Gynecol* 2015;126:575–84.
33 Groene SG, Tollenaar LSA, Slaghekke F, *et al*. Placental characteristics in monochorionic twins with selective intrauterine growth restriction in relation to the umbilical artery Doppler classification. *Placenta* 2018;71:1–5.
34 Yoon S, Jin Y, Kim Y, *et al*. Effect of delayed cord clamping on maternal and neonatal outcome in twin pregnancies: a retrospective cohort study. *Sci Rep* 2023;13:17339.