Universiteit Leiden
The Netherlands

Twin-to-twin transfusion syndrome : from placental anastomoses to long term outcome

Lopriore, E.

Citation
Lopriore, E. (2006, September 13). *Twin-to-twin transfusion syndrome : from placental anastomoses to long term outcome*. Retrieved from https://hdl.handle.net/1887/4556

Version:	Corrected Publisher's Version
License:	Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden
Downloaded from:	https://hdl.handle.net/1887/4556

Note: To cite this publication please use the final published version (if applicable).

Chapter 7

Hemoglobin differences at birth in monochorionic twins without chronic twin-to-twin transfusion syndrome

Enrico Lopriore MD
Marieke Sueters MD
Johanna M Middeldorp MD
Frank PHA Vandenbussche MD PhD
Frans J Walther MD PhD

Prenat Diagn 2005; 25:844-50

Abstract

Objectives: To determine the hemoglobin (Hb) differences at birth in monochorionic (MC) twins without chronic twin-to-twin transfusion syndrome (TTTS) in relation to birth order and placental vascular anatomy.

Methods: All consecutive cases of MC twins without chronic TTTS and dichorionic (DC) twins delivered at our center and admitted to our neonatal nursery between June 2002 and December 2004 were included in our study. We analyzed Hb differences at birth and on day 2, in relation to birth order and placental vascular anatomy.

Results: Forty-five pairs of MC twins and 71 pairs of DC twins were included. Mean Hb differences at birth in MC and DC twins were similar, 1.5 and 1.4 g/dL, respectively. Hb differences > 5 g/dL at birth were found in 2% (1/45) of MC twins compared to 8% (6/71) in DC twins. On day 2, mean Hb differences in MC twins increased to 3.8 g/dL, and the rate of MC twins with Hb differences > 5 g/dL increased to 27% (12/45) ($p < 0.001$). Mean Hb differences and the percentage of twins with Hb differences > 5 g/dL in DC twins did not change on day 2.
In MC twins, Hb levels measured on day 2 were significantly higher in second-born twins than in first-born twins, 17.7 and 15.5 g/dL, respectively ($p = 0.002$). Hb differences on day 2 were significantly higher in MC twins with superficial vascular anastomoses than those without superficial anastomoses, 4.0 g/dL and 1.5 g/dL, respectively ($p = 0.036$).

Conclusions: Hb differences occur more frequently in MC twins without chronic TTTS than in DC twins, but only when measured on the second day of life. Hb differences in MC twins are associated with birth order and superficial vascular anastomoses.

Introduction

Placental vascular anastomoses are almost invariably present in monochorionic (MC) twin gestations, but are extremely rare in dichorionic (DC) twin gestations[5]. In contrast to DC twins, MC twins are therefore at risk for twin-to-twin transfusion syndrome (TTTS). Several forms of TTTS have been described: chronic TTTS, acute perimortem TTTS and acute perinatal TTTS[11;30;42;45]. The chronic form of TTTS is the most common form and complicates about 15% of monochorionic twin pregnancies. Chronic TTTS occurs during the second or early third trimester of pregnancy due to unbalanced blood flow from one twin to the other through placental vascular anastomoses[8;108]. The recipient twin gradually becomes hypervolemic, polyuric, and develops polyhydramnios, whereas the donor twin becomes hypovolemic, oliguric and develops oligohydramnios. The pathogenesis of chronic TTTS is mainly mediated through deep arterio-venous anastomoses, in the absence of compensatory superficial arterio-arterial anastomoses[62]. Acute perimortem TTTS occurs in MC twins after intrauterine death of the co-twin. This form of acute TTTS results from acute exsanguination from the surviving twin into the low-pressure circulation of the demised co-twin through superficial arterio-arterial or veno-venous anastomoses and leads to severe hypoxic-ischemic injury in the surviving twin[13;30-32;70;217]. Risk of neurological handicap or death in the surviving twin is then extremely high [11;13;14]. Acute TTTS is also reported to occur in MC twins during labor, hence referred to as acute perinatal TTTS[34;40-44;218]. Acute perinatal TTTS is thought to result from uterine contractions or changes in fetal position leading to inter-twin blood pressure differences and inter-twin blood transfusion[36;44;45]. Rapid transfer of blood from the donor twin into the circulation of the recipient twin is probably mediated through superficial arterio-arterial or veno-venous anastomoses[71]. Acute perinatal TTTS may then lead to hemoglobin (Hb) differences at birth without necessarily discordance in birth weight[39;43]. So far, knowledge on acute perinatal TTTS is mainly speculative and based on case reports[34-39].

In 1972, Klebe and Ingomar hypothesized that Hb difference in MC twins at birth may be due to differences in placental blood transfusion in relation to birth order[38]. They postulated that once the umbilical cord of the first-born

twin is clamped, the second-born twin may not only receive blood from its own placenta but also from the placenta-share of the co-twin, through the patent vascular anastomoses. Other authors also share this opinion[35;41;44]. The aim of this study was to determine the Hb differences and hemodynamic disturbances at birth in MC twins without chronic TTTS and DC twins in relation to birth order, and establish if there was an association between Hb differences and the presence or absence of superficial vascular anastomoses.

Materials and methods

All consecutive cases of MC twins without chronic TTTS and DC twins delivered at our obstetrical department and admitted to our neonatal nursery between June 2002 and December 2004 were included in our study. The prenatal diagnosis of chronic TTTS was made by using standard ultrasound criteria[105]: 1.) Monochorionicity established by absence of a "twin peak" sign and the presence of a thin dividing membrane, 2.) Oligohydramnios (deepest vertical pocket ≤ 2cm) in the twin sac of one fetus, and 3.) Polyhydramnios (deepest vertical pocket ≥ 8cm before 20 weeks of gestation or ≥ 10cm after 20 weeks of gestation) in the twin sac of the other fetus. Monochorionicity was confirmed by histopathological examination of the placenta. Placental vascular anastomoses in MC placentas were studied by injection with colored dye (blue or green for arteries, yellow or orange for veins). Arterio-venous anastomoses were classified as deep anastomoses, whereas arterio-arterial and veno-venous anastomoses were classified as superficial anastomoses.
We excluded pregnancies complicated by maternal red blood cell alloimmunization, major fetal congenital malformations, higher multiples gestations, and twin gestations with intrauterine fetal death of a co-twin. The following obstetrical data were collected: gestational age at delivery, mode of delivery and time interval (in minutes) between delivery of twin 1 and twin 2. The following neonatal data were gathered: birth weight, Apgar score at 5 minutes, arterial blood pressure measured by Dinamap at birth and heart rate at birth. Renal function was assessed by measuring urine output during the first 24 hours after birth (in ml/kg/h). Growth

discordance was calculated by dividing the difference in birth weights by the birth weight of the larger twin. Hb levels were assessed at birth from umbilical cord blood. Since Hb levels are not reliable when measured shortly after acute shifts in blood volume, a second (venous) Hb level was analyzed on the second day of life, when clinically indicated[39;46;219;220]. Inter-twin Hb difference was defined as absolute Hb difference (higher Hb value minus lower Hb value). Inter-twin Hb differences were analyzed in relation to birth order (twin 1 versus twin 2) and in relation to birth weight (smaller twin versus larger twin). We recorded the use of blood transfusions during the first and second day of life, as well as the need for volume expanders and inotropic support during the first day of life. For the purpose of our study we defined acute perinatal TTTS in MC twins as an Hb difference of at least 5 g/dL at birth, without an obvious other cause for such difference. Acute hemorrhagic hypovolemic shock was defined as a combination of pallor, tachycardia (heart rate >160 bpm) and/or hypotension, requiring treatment with volume expanders, blood transfusion and/or inotropic support [220]. Hypotension was defined as a systolic blood pressure below the 3rd percentile for gestational age[221]. Serial cranial ultrasound scans were performed routinely in all neonates. Periventricular hemorrhage (grade classification according to Papile[222]) and cystic periventricular leucomalacia (grade classification according to de Vries[223]) were recorded. Other significant neonatal problems were also reviewed, including respiratory distress syndrome, chronic neonatal lung disease, patent ductus arteriosus, necrotizing enterocolitis, retinopathy of prematurity and hyperviscosity syndrome. We also recorded the total number of days during which phototherapy treatment was required.

Results of categorical variables were compared using Fisher's exact test or Chi-square test, as appropriate. McNemar's test was used for analysis of paired nominal data. The paired Student's *t* test was used to study normally distributed values within twin pairs, whereas the unpaired Student's *t* test was used to compare normally distributed values between two groups. The Spearman rank correlation was used to study the relationship between time-interval at birth between twin 1 and twin 2 and Hb differences between both infants. A p-value < 0.05 was considered to indicate statistical significance. Analysis was performed using SPSS version 11 (SPSS, Inc., Chicago, Illinois, USA).

Results

During the study period 1699 neonates were admitted to our nursery, among which 21% (349/1699) were born from 174 multifetal gestations. 55% (95/174) of the multifetal pregnancies were MC, and 45% (79/174) were DC. The Leiden University Medical Center is a tertiary medical center and serves as the national referral center for fetal invasive therapy in the Netherlands, which explains the high percentage of MC multifetal gestations and red blood cell immunization compared to other academic centers. A total of 45 MC pregnancies without chronic TTTS and 71 DC pregnancies were included in our study. The derivation of the included and excluded twin pregnancies is shown in Figure 1. Reasons for admission to our neonatal nursery were all mainly related to prematurity. Perinatal death did not occur in any of the MC twins without chronic TTTS delivered at our center during the study period.
Patients' characteristics for both MC and DC infants are shown in Table 1. There were no significant differences in baseline characteristics between the two groups, except for a higher percentage of MC infants being delivered by cesarean section compared to DC infants, 38% (34/90) versus 23% (32/142), respectively (p = 0.012). The percentage of MC and DC twin pairs with birth weight discordance > 20% was similar, 27% (12/45) and 24% (17/71), respectively.

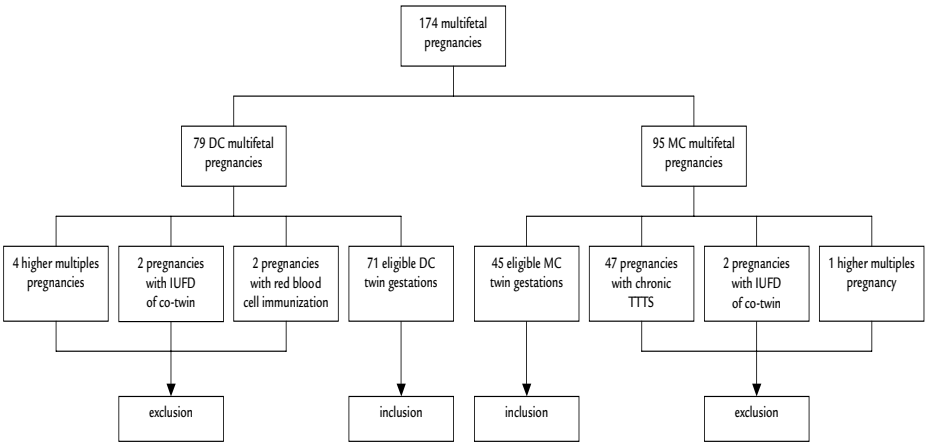

FIGURE 1 Flowchart showing the selection of our study population. (IUFD: intrauterine fetal demise)

TABLE 1 Baseline characteristics.

	MC infants (n = 90)	DC infants (n = 142)	p-value
Gestational age at birth – wk[a]	33.5 ± 3.4	32.6 ± 3.6	ns
Birth weight – g[a]	2040 ± 684	1885 ± 636	ns
Birth weight difference - %[a]	14 ± 11	13 ± 10	ns
Female – no. (%)	44 (49%)	72 (51%)	ns
Cesarean section – no. (%)[b]	34 (38%)	32 (23%)	0.012
Median Apgar score at 5 min (range)	9 (5-10)	9 (4-10)	ns
Neonatal death – no. (%)	3 (3%)	8 (6%)	ns
Respiratory distress syndrome – no. (%)	21 (23%)	46 (32%)	ns
Patent ductus arteriosus – no. (%)	5 (6%)	8 (6%)	ns
Periventricular hemorrhage grade 2-4 – no. (%)	2 (2%)	7 (5%)	ns

[a] *Value given as mean ± SD*
[b] *Refers to infants rather than mothers*

Hb values and hemodynamic parameters of MC and DC infants are presented in Table 2. Hb was measured at birth in 98% (88/90) and 93% (132/142) of MC and DC infants, respectively. On day 2, Hb measurements were available in 81% (73/90) and 85% (121/142) of MC and DC infants, respectively. Hb levels on day 2 were extracted from full blood count measurements, usually required to rule out perinatal infection associated with prematurity. Mean Hb differences at birth in MC twins and DC twins

TABLE 2 Hb values and hemodynamic parameters in MC and DC infants.

	MC infants (n = 90)	DC infants (n = 142)	p-value
Hb at birth[a]	16.5 ± 2.1	16.6 ± 2.3	ns
Hb difference between twins at birth[a]	1.5 ± 1.4	1.4 ± 1.7	ns
Hb on day 2[a]	16.6 ± 3.0	16.1 ± 2.6	ns
Hb difference between twins on day 2[a]	3.8 ± 2.5	1.7 ± 1.8	< 0.001
Hb difference >5 g/dl at birth – no. (%)	2 (2%)	12 (8%)	ns
Hb difference >5 g/dl on day 2 – no. (%)	24 (27%)	6 (4%)	< 0.001
Blood transfusion on day 1 or 2 – no. (%)	3 (3%)	9 (6%)	ns
Hypotensive at birth – no. (%)	9 (10%)	27 (19%)	ns
Volume expanders at birth – no. (%)	12 (13%)	31 (22%)	ns
Inotropic drugs – no. (%)	11 (12%)	14 (10%)	ns
Acute hemorrhagic hypovolemic shock – no. (%)	0 (0%)	0 (0%)	–

[a] *Value given as mean ± SD*

were similar, 1.5 and 1.4 g/dL, respectively. Hb differences > 5 g/dL at birth were found in 2% (1/45) of MC twin pairs compared to 8% (6/71) of DC twin pairs. On day 2, mean Hb differences in MC twins increased to 3.8 g/dL ($p < 0.001$). The rate of MC twin pairs with Hb differences > 5 g/dL increased up to 27% (12/45) ($p < 0.001$). In DC twins, mean Hb differences and percentage of twin pairs with Hb differences > 5 g/dL did not change on day 2.

Birth weight discordance > 20% and Hb difference > 5 g/dL at birth was detected in one pair (2%) of MC twins and in one pair (1%) of DC twins, in which the higher Hb level was found in the larger infant. In another set of DC twins with birth weight discordance > 20% and Hb difference > 5 g/dL at birth, the higher Hb level was found in the smaller twin. No difference in hemodynamic parameters, including blood pressure, heart rate, diuresis, or treatment with volume expanders, inotropics or blood transfusion, was found between MC and DC twins. None of the twins in our study suffered from acute hemorrhagic hypovolemic shock at birth. Serial cranial ultrasound scans showed a similar rate of periventricular hemorrhage (grade 2 to 4) in MC and DC twins, 2% (2/90) and 5% (7/142), respectively. None of the twins in both groups had cystic periventricular leucomalacia. One second-born infant of a preterm MC pregnancy required an exchange transfusion for hyperbilirubinemia on day 2 (serum bilirubin level: 13.9 mg/dL) despite phototherapy and adequate fluid administration. Routine work-up for hyperbilirubinemia showed an increase in Hb level from 14.3 g/dL at birth to 18.4 g/dL on day 2 without evidence of hemolysis and dehydration, suggesting that hyperbilirubinemia may have resulted from a high red cell volume.

Differences in Hb values and hemodynamic parameters in relation to birth order are presented in Table 3. A fall in Hb between birth and day 2 was found in first-born MC twins (- 0.9 g/dL), first-born DC twins (- 0.6 g/dL) and second-born DC twins (- 0.3 g/dL). A rise in Hb between birth and day 2 was found only in second-born MC twins (+ 1.1 g/dL). Mean Hb concentrations on day 2 in second-born MC twins on day 2 were significantly higher than in first-born MC twins, 17.7 and 15.5 g/dL, respectively ($p = 0.002$). No association between birth order and Hb differences was detected in DC twins. The fall in Hb between birth and day 2 in first-born MC twins was of similar magnitude as the fall in Hb in first-

TABLE 3 Hb values and hemodynamic parameters in MC and DC twin pairs in relation to birth order.

	MC twin pairs (n = 45)			***DC twin pairs (n = 71)***		
	Twin 1	Twin 2	p-value	Twin 1	Twin 2	p-value
Hb at birth[a]	16.4 ± 1.8	16.6 ± 2.4	ns	16.6 ± 2.4	16.6 ± 2.3	ns
Hb on day 2[a]	15.5 ± 2.2	17.7 ± 3.3	0.002	16.0 ± 2.6	16.3 ± 2.5	ns
Heart frequency at birth (bpm)[a]	150 ± 15	146 ± 19	ns	151 ± 18	151 ± 13	ns
Mean blood pressure at birth (mmHg)[a]	39.2 ± 7.4	38.8 ±7.9	ns	36.7 ± 7.7	35.3 ± 7.5	ns
Urine output on day 1 (ml/kg/h)[a]	2.7 ± 1.3	2.9 ± 1.3	ns	2.2 ± 1.1	2.3 ± 1.1	ns
Blood transfusion on day 1 or 2 – no. (%)	1 (2%)	2 (4%)	ns	6 (4%)	3 (2%)	ns
Volume expanders on day 1 – no. (%)	6 (13%)	6 (13%)	ns	16 (11%)	15 (11%)	ns
Inotropic drugs on day 1 – no. (%)	5 (11%)	6 (13%)	ns	7 (5%)	7 (5%)	ns
Phototherapy days[a]	1.7 ± 2.5	2.1 ± 2.7	ns	2.5 ± 3.0	2.5 ± 2.9	ns

[a] *Value given as mean ± SD*

born DC twins (p = 0.129), but was of greater magnitude compared to the fall in Hb in second-born DC twins (p = 0.028).

In MC twins, mean Hb values in the smaller and larger twin were respectively 16.3 and 16.8 g/dL (p = 0.065) at birth, and 16.7 and 16.4 g/dL (p = 0.753) on day 2. In DC twins, mean Hb values in the smaller and larger twin were respectively 16.8 and 16.4 g/dL (p = 0.148) at birth, and 16.3 and 16.0 g/dL (p = 0.303) on day 2.

Histopathological examination of MC placentas confirmed monochorionicity in all cases. Information on the type of vascular anastomoses was obtained in 80% (36/45) of the MC placentas. Arterio-arterial anastomoses, veno-venous anastomoses and arterio-venous anastomoses were present in 83% (30/36), 14% (5/36) and 83% (30/36) of placentas, respectively. Superficial vascular anastomoses were present in 83% (30/36) of MC placentas and absent in 17% (6/36) of MC placentas. Differences in Hb values in MC twin pairs with and without superficial vascular anastomoses are presented in Table 4. Mean Hb differences on day 2 were significantly higher in MC with superficial anastomoses than in MC twins without superficial vascular anastomoses, 4.0 g/dL and 1.5 g/dL, respectively (p = 0.036). Hb differences > 5 g/dL on day 2 were detected in 27% (8/30) of MC twin pairs with superficial anastomoses and 16% (1/6) of MC twin pairs without superficial anastomoses. There was no significant association between Hb differences > 5 g/dL and superficial vascular anastomoses probably because of the small number of cases.

TABLE 4 Hb values in MC twin pairs with and without superficial vascular anastomoses.

	Twin pairs with superficial anastomoses (n = 30)	Twin pairs without superficial anastomoses (n = 6)	p-value
Hb difference at birth[a]	1.3 ± 1.3	1.3 ± 1.3	ns
Hb difference on day 2[a]	4.0 ± 2.2	1.5 ± 1.6	0.036
Hb difference >5 g/dl at birth – no. (%)	0 (0%)	0 (0%)	–
Hb difference >5 g/dl on day 2 – no. (%)	8 (27%)	1 (16%)	ns

[a] *Value given as mean ± SD*

The median time interval between delivery of twin 1 and twin 2 in the sub-group of MC twins delivered vaginally was 5 minutes (range 1-40 minutes). We found a positive correlation between time interval between vaginal delivery of the first and second-born infants and Hb differences on day 2 (Spearman correlation coefficient = 0.402), but the increase in Hb differences was not significant (p = 0.079). No correlation was found between time interval between vaginal delivery of the first and second-born infants and Hb differences at birth. The difference in mean Hb concentrations between MC twins born vaginally and through caesarean section was not significant, respectively 1.7 versus 1.2 g/dL at birth (p = 0.355) and 3.7 versus 3.9 g/dL on day 2 (p = 0.778).

Comment

This study shows that Hb differences at birth between MC twins without chronic TTTS and DC twins are similar. Only a small number of twin pairs in both groups of twins have highly discordant Hb values (Hb difference > 5 g/dL) at birth. However, when Hb levels are measured on day 2, Hb differences between MC twins become more evident and one in four MC twin pairs has Hb differences > 5 g/dL. The different Hb values between birth and day 2 may be due to acute shifts in blood volume in MC twins during delivery[39]. Hb concentrations are known to be unreliable when measured shortly after acute shifts in blood volume. When acute blood loss occurs, Hb levels may initially remain within the normal range and not reflect the actual blood loss[46;219;220]. After equilibration between

intravascular and extravascular spaces has completed, the expected fall in Hb levels may appear. This compensatory mechanism of equilibration or hemodilution may take several hours to complete[39;220;224]. Hemodilution is due to a gradual increase in plasma volume and intravascular volume to compensate for the blood loss. Conversely, when an infant receives an acute transfusion of blood, the infant responds by gradually decreasing its plasma volume while the red cell mass remains unchanged[224;225]. After equilibration between intravascular and extravascular spaces is complete, the expected rise in Hb levels may appear.

This study also establishes a clear association between Hb difference and birth order in MC twins. We found that Hb levels on day 2 were significantly higher in second-born MC twins than in first-born MC twins. Our results are in agreement with previous studies[35;38;46]. Once the umbilical cord of the first-born twin is clamped, the second twin has sole access to the entire placenta and may therefore receive blood through the vascular anastomoses from both parts of the placenta [38;41]. To determine whether the Hb difference in MC twins was due to a relatively higher Hb concentration in second-born twins or a lower Hb concentration in first-born twins, we compared Hb values between MC and DC twins. The fall in Hb between birth and day 2 found in first-born MC is also detected in first and second-born DC twins and is probably due to factors related to prematurity, such as blood loss caused by repeated venepunctures and hemodilution caused by treatment with volume expanders. The rise in Hb between birth and day 2 in second-born MC twins was in striking contrast to the fall in Hb in all other infants. Thus, Hb differences between MC twins are probably due to a relatively higher Hb in second-born twins rather than a lower Hb in first-born twins. The rise in Hb levels in second-born twins on day 2 compared to day 1 may reflect the process of hemoconcentration after acute blood transfusion. High red cell volume can be potentially harmful in neonates and lead to polycythemia or severe hyperbilirubinemia[224;225] requiring an exchange transfusion, as occurred in one second-born twin in our study.

We also report that Hb differences in MC twins measured on day 2 are greater in the presence of superficial vascular anastomoses. Superficial arterio-arterial and veno-venous anastomoses are known to be responsible for acute transfusions of blood after intrauterine fetal death of one of the

twins[30;32;70]. In analogy to acute perimortem TTTS, it is conceivable that superficial vascular anastomoses may also be responsible for rapid inter-twin blood transfusion during delivery. Hypothetically, after clamping of the first-born's cord, uterine contractions may allow placental blood from the first twin's low-pressure placental bed to be transfused through the low-resistance superficial vascular anastomoses into the higher pressure circulation of the second twin.

Disparity in placental blood transfusion may also be responsible for Hb differences in MC twins[38]. The amount of placental blood transfused into the circulation of the newborn before clamping of the umbilical cord is a major factor determining Hb levels[225]. Assuming that the time taken to clamp each of the umbilical cords is not different between twin 1and 2, other factors may be related to Hb differences in MC twins, such as mode of delivery or time interval between birth of twin 1 and 2. We detected no association between mode of delivery (vaginal delivery or cesarean section) and Hb differences in MC twins. A positive, but statistically not significant correlation was found between Hb differences and time interval between vaginal delivery of twin 1 and twin 2.

A weakness of our study is that we excluded all uncomplicated term or near-term twin deliveries, as Hb is obviously not routinely taken on term infants. Risk of significant acute perinatal transfusion in term MC twins remains therefore unknown and needs to be investigated in future studies.

A handful of case reports of MC twins with acute perinatal TTTS have been reported in the literature[34-39]. Most donor twins had signs of acute hemorrhagic hypovolemic shock and required prompt refilling of the intravascular compartment with blood transfusion or volume expanders. In our study, only one of the 45 pairs of MC twins fulfilled our criteria for acute perinatal TTTS and the donor twin had no characteristic signs of acute hemorrhagic hypovolemic shock, such as pallor, tachycardia and/or hypotension. Diagnostic criteria for acute perinatal TTTS vary among the published case reports, but always include a significant Hb difference at birth. Most reports also rely on the absence of birth weight discordance between both twins to exclude chronic TTTS[34;35;38;39]. However, birth weight and Hb discordance are not appropriate diagnostic criteria for chronic TTTS[11;27;28;71;93]. As shown in this study, birth weight discordance and Hb difference can also be found in DC twins and in MC

twins without antenatal signs of chronic TTTS. Moreover, Hb discordance is only present in a minority of cases with chronic TTTS[102]. Diagnosis of TTTS is nowadays based on antenatal ultrasound finding of the characteristic oligo-polyhydramnios sequence[11;27-29;93]. Therefore, most case reports in which acute perinatal TTTS was diagnosed without antenatal ultrasound examinations, may have been cases of chronic TTTS, the most common cause for hematological and hemodynamic discordance in MC twins[34;35;38;39]. Furthermore, acute shifts of blood volume in acute perinatal TTTS or acute perimortem TTTS may occur in any MC twins with patent vascular anastomoses, with or without birth weight discordance.
Differential diagnosis of acute perinatal TTTS should not only include chronic TTTS, but also acute perimortem TTTS. In one case report of acute perinatal TTTS, the hyperperfused recipient twin died during delivery and the hypoperfused donor died postnatally due to acute renal failure[36]. However, pathologic examination showed chorioamnionitis and funisitis, and culture of the placenta grew a *Fusobacterium* species. Therefore, acute perimortem TTTS due to bacterial sepsis seems a more plausible explanation for the hematological and hemodynamic discordance at birth rather then acute perinatal TTTS.
The pathogenesis of acute perinatal TTTS remains unclear. Superficial vascular anastomoses have been suggested to be responsible for acute perinatal blood transfusions[71]. The association between Hb differences and superficial vascular anastomoses reported in this study is in agreement with this suggestion. Acute fetal blood loss from the donor twin into the circulation of the recipient twin may then occur as a result of variations in blood pressure due to uterine contractions or fetal positions, but strong evidence is not available. Birth order may also play a major role in the etiology of acute perinatal TTTS. Uotila and Tammela treated three cases with acute perinatal TTTS during a 2-year period[37]. In all three cases, the donor twin was the second-born twin. The authors therefore hypothesized that acute hemorrhagic hypovolemic shock may result from acute feto-placental transfusion from the second-born twin into the placenta due to decreased vascular resistance in the placenta-share of the first twin. Although the number of MC twins born at our hospital during the study period is almost certainly higher than the number reported by Uotila and Tammela, similar events were never recorded at our center. Moreover, most

authors suggest that after clamping the cord of the first-born twin, second-born twins are more likely to receive a large placental blood transfusion rather than lose blood into the placenta[35;38;41]. Our findings also support this hypothesis, since second-born twins had significantly higher Hb values than first-born twins.

We conclude that significant Hb differences are often found in MC twins without chronic TTTS, especially when Hb measurements are performed on day 2. Hb differences in MC twins are related to birth order and superficial vascular anastomoses.