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The impact of placental anastomoses and umbilical cord insertions' sites on monochorionic twin pregnancy outcomes: Evidence from color-dye injection studies

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ABSTRACT

Introduction: Our knowledge of monochorionic pregnancies' complications is largely based on the extensive ongoing research on monochorionic placental structure. Previous studies on the concordance of umbilical cord insertions are limited. This study aimed to evaluate placental anastomoses and cord insertions as independent risk factors for neonatal adverse outcomes.

Methods: This was a prospective study conducted at Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy from April 2021 to December 2022. Seventy-six women with a monochorionic pregnancy were enrolled at their first-trimester scan. After delivery, all placentas that were confirmed to be monochorionic were analyzed according to standard protocols, including those of complicated monochorionic twin pregnancies. The primary outcomes were a Composite Monochorionic Pregnancy Outcome (CMPO) and a Composite Neonatal Adverse Outcome (CNAO). The secondary outcome was the birth weight discordance between the neonates.

Results: The CMPO occurred in 15.8 % pregnancies, and the CNAO occurred in 67.1 % pregnancies. The analysis confirmed a significant association between velamentous cord insertions and neonatal adverse events ($p = 0.003$). Also, a significant positive association ($p = 0.0326$) between twin birth weight discordance and discordance in twins umbilical cord insertions' sites was found. No significant association between the number and type of the anastomoses and both the CMPO or CNAO was detected.

Discussion: Our data suggest that the routine sonographic assessment of umbilical cords' insertion sites during the first trimester could be helpful in predicting fetal and neonatal adverse events. We believe that this sonographic assessment should start to be implemented in our routine care of monochorionic pregnancies.

1. Introduction

The last five decades have witnessed a huge growth in twin pregnancy rate, with an increase by about 70 % in fifty years [1]. This incidence is steadily increasing as a direct result of the increase in maternal age and the spread of Artificial Reproductive Technologies (ART) [2]. Among these, monochorionic (MC) pregnancies represent a challenge in obstetric practice. Not only are all twin pregnancies associated with a higher risk of all maternal-fetal complications of pregnancy, but the peculiar angioarchitecture of MC twins' placentas is also responsible for unique complications that cause higher odds of perinatal morbidity and mortality as compared to dichorionic (DC) twins and singletons [3–6], like Twin-to-Twin Transfusion Syndrome (TTTS), Twin Anemia-Polycythemia Sequence (TAPS), selective Intrauterine Growth Restriction (sIUGR), and Twin Reversed Arterial Perfusion Syndrome (TRAP). Also, the condition of sharing the placenta warrants different management from common problems in multiple gestation, such as growth restriction of one twin or discordant structural

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anomalies, because the well-being of the twins is interrelated and each twin is exposed to the environment of its cotwin [7]. An equal division of the single shared placenta is essential to ensure a comparable supply of nutrients and oxygen between both twins, and several studies suggest that unequal placental sharing is the most important risk factor for sIUGR [8,9].

Our knowledge of MC pregnancies complications is largely based on the extensive ongoing research on MC placental structure. In particular, a growing body of literature has evaluated the prevalence of placental vascular anastomoses through color-dye injection studies of MC placentas after delivery [8,10]. Without understanding the role of placental anastomoses and placental sharing, we would not be able to manage and treat the above-mentioned conditions.

The present study is a preliminary attempt to further broaden current knowledge of the pathophysiology implicated in MC pregnancy adverse events. We have been focused on placental characteristics, such as vascular anastomoses and cord insertions, studied as independent risk factors for fetal and neonatal adverse outcomes. An early recognition of risk factors predictive of adverse neonatal outcome could potentially represent an additional diagnostic tool in order to improve the clinical management of these challenging pregnancies. In addition, this study aims to validate global findings regarding prevalence and role of these placental characteristics in a specific Italian cohort of patients.

2. Methods

This was a prospective study conducted between April 2021 and December 2022 at Fondazione Policlinico Universitario Agostino Gemelli IRCCS, a tertiary medical center for perinatal medicine in Rome, Italy. The study aimed to compare the incidence of fetal and neonatal adverse events between different groups of patients with a monochorionic twin pregnancy classified according to umbilical and placental characteristics.

The study was approved by the Department Internal Board (#DIPUSVSP-16-11-2086) and by the Ethics Committee under the protocol "*Twin pregnancy: a challenge for patients, families and health professionals*" (ID 3797), which is registered on the ClinicalTrials.gov public website (identifier NCT05761769).

All eligible pregnant women carrying viable twins with ultrasound evidence of a MC placenta were prospectively enrolled at their first-trimester scan (n = 79) (Fig. 1). At the first scan, there were no signs of complications such as TTTS, TAPS, sIUGR, or TRAP. Hence, each monochorionic twin pregnancy began as an uncomplicated pregnancy. The distinction between monochorionic-monoamniotic (MCMA) and monochorionic-biamniotic (MCBA) pregnancies was meticulous achieved through examination of the interamniotic septum during the first-trimester abdominal ultrasound. In cases where diagnostic certainty remained elusive, transvaginal ultrasound was employed to enhance precision and conclusiveness. Patients consented to placental examination under the study protocol. Demographic and obstetrical data were obtained throughout the pregnancy. In accordance with our internal protocol, in the absence of any additional clinical-obstetrical indications, monochorionic-biamniotic pregnancies were either scheduled for induction or elective cesarean section (CS) at 36 weeks. After delivery, the placentas were stored at 4 °C until color-dye injection and examined within 7 days. Chorionicity was confirmed by gross examination of the dividing membrane and/or histopathological examination of the placenta and the dividing membrane. The umbilical cord of each twin was catheterized and injected with color dye following the method described by Lewi et al. (2013) [11]. Data on umbilical cords' insertions, and presence, number, and type of anastomoses, was collected.

We excluded higher multiple pregnancies (n = 2) and pregnancies which appeared to be DC after chorionicity confirmation (n = 1). When analyzing the anastomoses, we also excluded the patients whose placentas could not be injected (n = 10) because of tissue disruption, erroneous shipment in formaldehyde, or unlabeled cords.

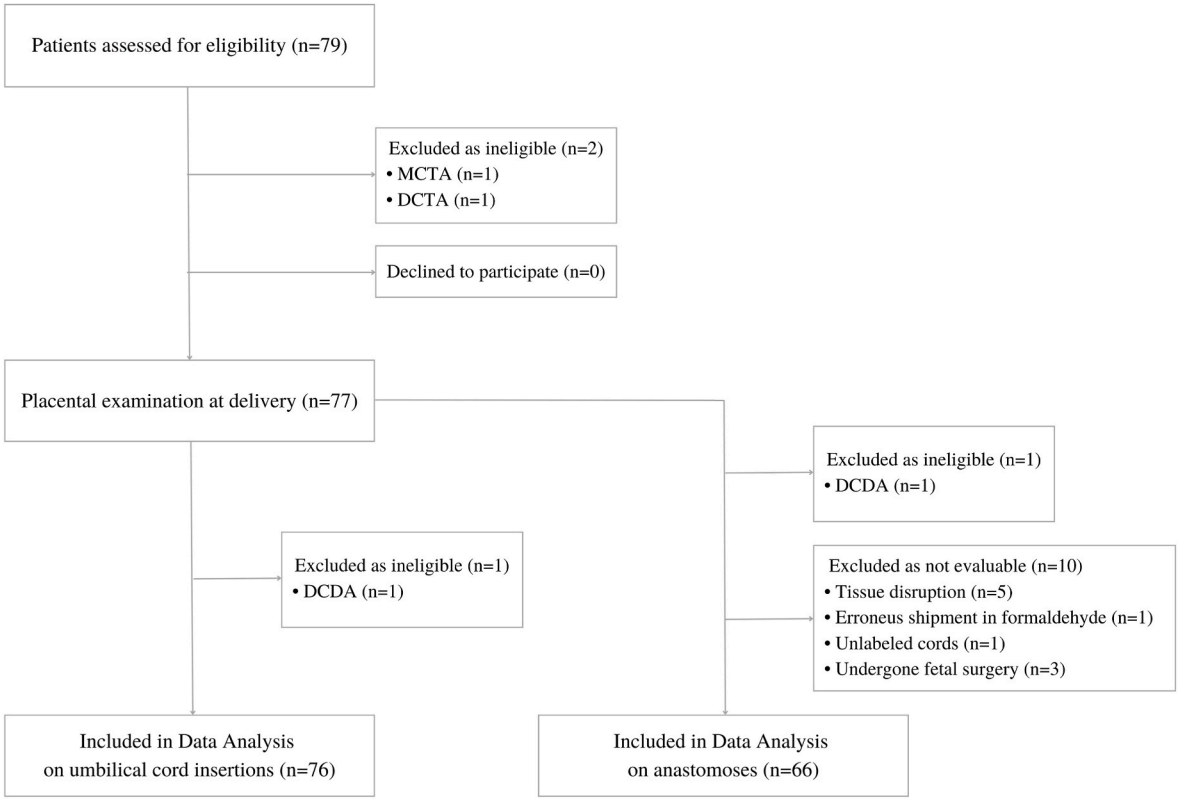

Fig. 1. Design and flow of participants through the study. MCTA = Monochorionic Triamniotic; DCTA = Dichorionic Triamniotic; DCDA = Dichorionic Diamniotic.

The primary outcomes of the study were a Composite Monochorionic Pregnancy Outcome (CMPO) and a Composite Neonatal Adverse Outcome (CNAO). While we acknowledge that the included complications may vary in terms of severity and clinical impact, the use of a composite outcome provides a practical approach to capture a range of relevant outcomes given our sample size. The secondary outcome of the study was the birth weight discordance between the neonates.

The composite outcome for complications in MC twin pregnancies, termed CMPO, encompassed four conditions: TTTS, TAPS, sIUGR, and TRAP. CMPO was defined as 1 if at least one of these four complications was present, and 0 if none were observed. TTTS diagnosis followed the Quintero staging system [12]. The recipient twin was identified by the presence of polyhydramnios (maximum deepest vertical pocket of amniotic fluid ≥8 cm before 20 weeks of gestation or ≥10 cm after 20 weeks of gestation), while the donor twin was determined by oligohydramnios (maximum deepest vertical pocket of amniotic fluid ≤2 cm). TAPS diagnosis relied on both fetal and neonatal criteria [13]. Fetal TAPS was identified through Doppler ultrasound evaluation of the middle cerebral artery (MCA) peak systolic velocity (PSV) measurements in both twins. TAPS was diagnosed when the Delta PSV-ACM (difference in MCA-PSV between the twins) was 0.5 MoM or more. Neonatal TAPS was diagnosed based on significant hemoglobin discordance (≥7 g/dL) and reticulocyte discordance (>15 %) between the donor and recipient twin. sIUGR was defined by either an Estimated Fetal Weight (EFW) below the 3rd percentile for gestational age in one twin, or the presence of two out of the following three criteria: EFW below the 10th percentile, pulsatility index of the umbilical artery (PI-AO) above the 95th percentile, and abdominal circumference (CA) below the 10th percentile. Additionally, a weight discrepancy exceeding 25 % between the twins is considered another criterion for sIUGR diagnosis [14].

CNAO is a binary composite outcome for fetal and neonatal adverse events which includes neonatal mortality, Neonatal Intensive Care Unit (NICU) admission, Small for Gestational Age (SGA) defined as birthweight below the 10th percentile for babies of the same gestational age, Respiratory Distress Syndrome (RDS), Apgar <7 at 5 min, Intraventricular Hemorrhage (IVH), Intubation and ventilation for at least 24 h, Tube feeding for at least 4 days, Intrauterine Fetal Demise (IUFD), Hypotonia for at least 2 h, Stupor/coma. CNAO was defined as 1 if there has been at least one of these complications in at least one twin, or 0 if there has been none.

Concerning the placental characteristics, umbilical cord insertions were classified as “normal“ (e.g. central, paracentral, eccentric), “marginal” (distance <2 cm), and “velamentous” (Fig. 2), according to placental pathology reports [15]. Then, each placenta was further classified into three categories based on the combination of umbilical cord insertions: concordant placentas (both cords normal, both marginal, or both velamentous), intermediate placentas (comprising normal-marginal cords or marginal-velamentous cords), and discordant placentas (featuring normal-velamentous cords) [16]. Umbilical cords’ distance, which represented the spatial gap between the attachment points of each umbilical cord to the placenta, was measured in centimeters by considering the closest edges of both cords. Finally, placental anastomoses were classified in: Arterio-Arterial (AA), Arterio-Venous (AV), Veno-Arterial (VA), and Veno-Venous (VV). AA and VV anastomoses are superficial and bidirectional, forming direct communications on the surface of the chorionic plate. On the contrary, AV and VA anastomoses are deep and unidirectional anastomoses.

Descriptive statistics were done by using absolute and relative frequencies for categorical variables, while mean and standard deviations (SD) were reported for numerical ones.

The number of subjects who had at least one MC pregnancy complication (CMPO) and neonatal adverse event (CNAO) was calculated. Moreover, the association between the clinical outcomes (CMPO, CNAO) and the placental characteristics (number and type of anastomoses, cord insertions’ sites, cord insertions’ distance) was evaluated using chi-square/Fisher test or *t*-test, as appropriate. Association between birth weight discordance and placental characteristics was also evaluated using ANOVA and correlation (r) tests.

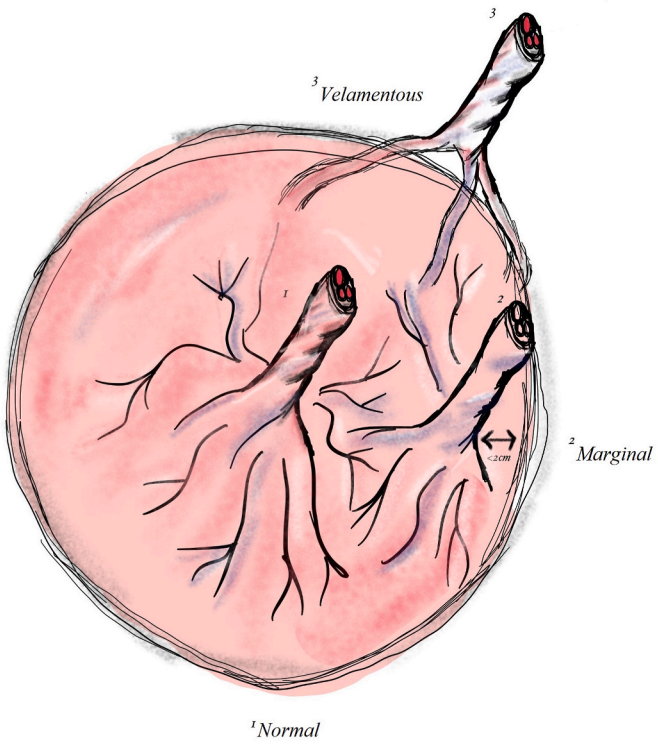

Fig. 2. Types of umbilical cord insertions.

All the analysis was conducted using the software SAS 9.4 and statistical threshold was set at 0.05 (two-tailed).

3. Results

After chorionicity confirmation at delivery, seventy-sixty patients were considered eligible for inclusion. Of the 76 patients eligible for inclusion, 72 (94.7 %) had an MC diamniotic (DA) pregnancy and 4 (5.3 %) had an MC monoamniotic (MA) pregnancy. No patients withdrew their consent to participate in the study and no patients were lost to follow-up.

The baseline characteristics of the entire cohort are summarized in Table 1. Of the 76 patients included in the study, 71 (94.7 %) were Caucasian. The average age of the entire cohort of patients was 34.0 ± 5.5 years (range 19–51). Pre-pregnancy BMI ranged from 17.3 to 46.9 (mean 24.0 ± 5.7), with 8 (10.5 %) patients having a BMI >30 kg/m2. Regarding obstetric history, 40 (52.6 %) patients were primigravid. The mean gestational week at delivery was 34.3 ± 3.3 when considering the entire population, 34.8 ± 0.7 when considering only the group of pregnancies without velamentous cord insertions, and 31.7 ± 2.6 when considering the group of pregnancies with at least one velamentous cord insertion. Pregnancy was achieved through ART in 6 cases (7.9 %). Among the 76 patients in our study, 14 (18.4 %) experienced spontaneous labor before reaching 36 weeks of gestation, while 23 patients (30.2 %) required CS or labor induction prior to the 36-week threshold due to clinical-obstetrical indications such as sIUGR, hypertension, preeclampsia, and abnormal doppler findings. Additionally, in accordance with our protocol, 39 patients (51.3 %) underwent labor induction or CS at 36 weeks.

Past and current medical conditions are summarized in Table 1. Of note, 18 (23.7 %) patients had a history of smoking, 3 (4 %) patients had a history of diabetes mellitus, and 1 (1.3 %) patient had chronic hypertension. During pregnancy, 9 (11.8 %) patients developed gestational

Table 1
Baseline characteristics for the Entire Cohort.

Characteristic	*n = 76*
***Age**, years (mean ± SD)*	34.01 ± *5.5*
***Height**, cm (mean ± SD)*	165.0 ± *0.07*
***Pre- pregnancy BMI**, kg/m^2 (mean ± SD)*	23.99 ± *5.7*
***BMI* > 30 kg/m^2**, *n (%)*	8 (10.5)
***Weight gain in pregnancy**, kg (mean ± SD)*	14.26 ± *12.7*
***Caucasian**, n (%)*	71 (94.7)
***Primigravid**, n (%)*	40 (52.6)
***Nulliparae**, n (%)*	59 (77.6)
***Previous C-section**, n (%)*	10 (13.2)
***ART**, n (%)*	6 (7.9)
***Smoking**, n (%)*	18 (23.7)
***Thrombophilia**, n (%)*	2 (2.6)
***Chronic Hypertension**, n (%)*	1 (1.3)
***Epilepsy**, n (%)*	1 (1.6)
***Diabetes mellitus**, n (%)*	3 (4)
***Antiphospholipid syndrome**, n (%)*	0 (0)
***Nephropathy**, n (%)*	0 (0)
***Autoimmune disorder**, n (%)*	0 (0)
***Mental disorder**, n (%)*	0 (0)
***Spontaneous labor before 36 weeks**, n (%)*	14 (18.4)
***Induction of labor or CS before 36 weeks**, n (%)*	23 (30.2)
***Induction of labor or CS at 36 weeks**, n (%)*	39 (51.3)
***GDM**, n (%)*	9 (11.8)
***GHTN**, n (%)*	5 (6.6)
***Preeclampsia**, n (%)*	3 (4)
***Eclampsia**, n (%)*	0 (0)
***HELLP syndrome**, n (%)*	0 (0)

BMI = Body Mass Index; ART = Assisted Reproductive Technology; CS= Cesarean Section; GDM = Gestational Diabetes Mellitus; GHTN = Gestational Hypertension; HELLP = Hemolysis, Elevated Liver enzymes and Low Platelets syndrome.

Table 2
Incidence of analyzed complications.

Pregnancy Complication[a]		*n=76*
***sIUGR**, n (%)*		8 (10.5)
***TTTS**, n (%)*		6 (7.9)
***TAPS**, n (%)*		2 (2.6)
***TRAP**, n (%)*		0 (0)
Neonatal Complication	*At least one neonate (n=76)*	*Both neonates (n=76)*
***NICU admission**, n (%)*	20 (26.3)	18 (23.7)
***RDS**, n (%)*	19 (25)	10 (13.2)
***SGA**, n (%)*	31 (40.8)	5 (6.6)
***Neonatal death**, n (%)*	6 (7.9)	4 (5.3)
***Intubation and ventilation for at least 24 h**, n (%)*	7 (9.2)	4 (5.3)
***Tube feeding for at least 4 days**, n (%)*	6 (7.9)	4 (5.3)
***IUFD**, n (%)*	2 (2.6)	2 (2.6)
***Hypotonia for at least 2 h**, n (%)*	2 (2.6)	1 (1.3)
***Stupor/coma**, n (%)*	2 (2.6)	1 (1.3)
***IVH**, n (%)*	2 (2.6)	0 (0)
***Apgar at* 5 min < *7**, n (%)*	2 (2.6)	0 (0)

[a] Of note, 2 (2.63 %) patients developed both TTTS and sIUGR, one (1.32 %) patient developed both TTTS and TAPS, and 1 (1.32 %) patient developed both TAPS and sIUGR. sIUGR = Selective Intrauterine Growth Restriction; TTTS = Twin-to-Twin Trasfusion Syndrome; TAPS = Twin Anemia Policitemia Sequence; TRA P = Twin Reversed Arterial Perfusion; NICU = Neonatal Intensive Care Unit; RDS = Respiratory Distress Syndrome; SGA = Small for Gestational Age; IUFD = Intrauterine Fetal Death; IVH = Intraventricular Hemorrhage.

Diabetes Mellitus (GDM), 5 (6.6 %) patients developed Gestational Hypertension, and 3 (4 %) patients developed preeclampsia. There were no significant differences observed in the maternal characteristics examined (e.g., smoking history, diabetes mellitus, chronic hypertension, thrombophilia, nephropathy, epilepsy, mental illness, autoimmune diseases, asthma) between the group without velamentous insertion and the group with at least one velamentous insertion.

The rates of the analyzed complications are summarized in Table 2. Of the 76 patients enrolled, 12 patients (15.8 %) developed at least one complication. The incidence of sIUGR, TTTS and TAPS were respectively 10.5 % (8/76), 7.9 % (6/76), and 2.6 % (2/76). Regarding the cases of TTTS, out of the six cases identified, three cases (50 %) were considered eligible for and underwent laser ablation treatment. One of these cases subsequently experienced post-ablation TAPS, which was diagnosed thereafter. Of note, 2 (2.63 %) patients developed both TTTS and sIUGR, 1 (1.32 %) patient developed both TTTS and TAPS, and 1 (1.32 %) patient developed both TAPS and sIUGR. No case of Twin Reversed Arterial Perfusion (TRAP) sequence was reported (0 %).

When considering fetal and neonatal outcomes, 51 patients out of 76 (67.1 %) had at least one adverse event in at least one twin. Neonatal death of at least one twin occurred in 6 (7.9 %) patients. In 4 of these 6 cases, neonatal death of both twins occurred. Additionally, IUFD occurred in 2 patients (2.6 %). SGA of at least one twin occurred in 31 cases, while SGA of both neonates occurred in 5 cases. Also of note is the incidence of RDS and NICU admission in at least one twin, which were respectively 25 % and 26.3 %.

Placental characteristics, separated for CMPO presence or absence are summarized in Table 3. Concordant placentas accounted for 51.3 % of cases, whereas only 7 % of placentas were discordant. No cases of vasa previa were detected in our population, neither during our routine transvaginal ultrasound screening, nor at the time of delivery. The average umbilical distance in our cohort was 11.5 ± 5.50 cm (range 0–24 cm). Concerning the anastomoses, the most common type found was the AA (89.4 % of cases), followed by the AV (80.3 %), VA (74.2 %), and VV (28.8 %).

Results regarding the association between the studied placental characteristics and the presence of a CMPO or CNAO outcome are shown in Table 3. No significant association was found between the development of a CMPO and the presence of anastomoses ($p > 0.10$). Furthermore, no significant association was found between the development of a CMPO outcome and the umbilical cords' insertion sites. Strong evidence of the association between the type of umbilical cord insertion and feto-neonatal adverse events was found ($p = 0.003$). Normal cord insertions were the most common within the group without CNAO, while velamentous cord insertions were associated with the occurrence of at least one feto-neonatal adverse event in 100 % of cases. The analysis did not reveal any significant association between feto-neonatal adverse events and the presence of each type of anastomosis.

Results regarding the association between the placental characteristics and birth weight discordance revealed a significant association ($p = 0.03$): the mean value of birth weight discordance increases with increasing umbilical cord discordance. Particularly, the mean weight discordance was 0.10 (SD 0.07) for concordant placental, 0.12 (SD 0.08) for intermediate and 0.18 (SD 0.12) for discordant (Fig. 3). The correlation between birth weight discordance and cord insertions' distance is positive ($r = 0.1584$), but it is not statistically significant ($p = 0.2$). The presence or absence of different types of anastomoses was not significantly associated with an increase in birth weight discordance (see supplementary files).

4. Discussion

The analysis revealed that the CMPO occurred in 15.8 % (12/76) of pregnancies, while the CNAO occurred in 67.1 % (51/76) of pregnancies. Importantly, our analysis confirmed a significant association

Table 3
Placental characteristics and Primary outcomes.

Variable	*Total*	*CMPO (No) (n =64)*	*CMPO (Yes) (n =12)*	*p-value*	*CNAO (No) (n =25)*	*CNAO (Yes) (n =51)*	*p-value*
Placenta classification	***n = 76***			0.5897			0.1366
Concordant*, n (%)*	39 (51.3)	33 (51.6)	6 (50)		15 (60)	24 (47.1)	
Discordant*, n (%)*	7 (9.2)	5 (7.8)	2 (16.7)		0 (0)	7 (13.7)	
Intermediate*, n (%)*	30 (39.5)	26 (40.6)	4 (33.3)		10 (40)	20 (39.22)	
Umbilical insertion twin 1[a]	***n = 76***			0.2643			0.0324
Normal*, n (%)*	49 (64.5)	35 (70)	5 (50)		25 (78.1)	24 (60)	
Marginal*, n (%)*	16 (21)	10 (20	3 (30)		6 (21.9)	9 (22.5)	
Velamentous*, n (%)*	7 (9.2)	5 (10)	2 (20)		0 (0)	7 (17.5)	
Umbilical insertion twin 2[a]	***n = 76***			0.1927			0.1232
Normal*, n (%)*	38 (50)	25 (50)	6 (60)		18 (56.3)	20 (50)	
Marginal*, n (%)*	29 (38.2)	22 (44)	2 (20)		14 (43.8)	15 (37.5)	
Velamentous*, n (%)*	5 (6.6)	3 (6)	2 (20)		0 (0)	5 (12.5)	
Umbilical insertion[b]							0.0032
Normal*, n (%)*					43 (67.2)	44 (55)	
Marginal*, n (%)*					21 (32.8)	23 (28.8)	
Velamentous*, n (%)*					0 (0)	13 (16.3)	
Anastomoses	***n = 66***						
AA present*, n (%)*	59 (89.4)	45 (93.75)	6 (85.71)	0.1981	21 (95.5)	38 (86.4)	0.4094
VV present*, n (%)*	19 (28.8)	14 (29.17)	1 (14.29)	0.4215	5 (22.7)	14 (31.8)	0.5682
AV present*, n (%)*	53 (80.3)	38 (79.17)	6 (85.71)	<0.999	17 (77.3)	36 (81.8)	0.7464
VA present*, n (%)*	49 (74.2)	34 (70.83)	6 (85.71)	0.6689	19 (86.4)	30 (68.2)	0.1426
Umbilical cords distance*, mean (SD)*		11.39 (5.70)	12.05 (4.49)	0.7186	10.33 (5.39)	12.09 (5.51)	0.2134

AA = Artery-to-Artery; VV = Vein-to-Vein; AV = Artery-to-Vein; VA = Vein-to-Artery.
[a] Analyzed CNAO was only that of the neonate of interest.
[b] Umbilical insertions of twin 1 and twin 2 were considered as independent variables.

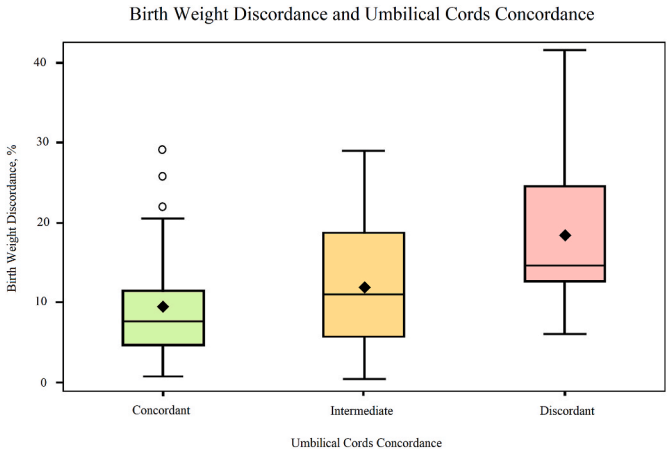

Fig. 3. "**Birth weight discordance and Umbilical Cords Concordance**". The box plot illustrates the relationship between umbilical cords concordance and birth weight discordance in the study population. Empty dots = outliers, which are those with a "Birth Weight Discordance" value exceeding the third quartile +1.5 times the interquartile range. Rhombuses = the means of "Birth Weight Discordance" for each "Umbilical Concordance" category. Error bars = 95 % confidence intervals.

between the type of umbilical cord insertion and feto-neonatal adverse events (p = 0.003). Additionally, we found a significant positive association (p = 0.03) between twin birth weight discordance and discordance in twins' umbilical cord insertion sites. No significant correlation was found between umbilical insertion discordance and adverse neonatal events. Similarly, no significant correlation between anastomoses and both the CMPO or CNAO was detected.

Comparing our results to existing literature, we found a noteworthy degree of correspondence in the incidence rates of MC complications. In particular, the incidence rates of TTTS, TAPS, sIUGR reported in the literature are respectively 10–15 %, 3–6%, 10–15 % [17–20], compared with respectively 7.9 %, 2.6 %, and 10.5 % of our cohort (Table 2). Of note, perinatal death of at least one twin occurred in 7.9 % of our cohort, and two twins were involved in 5.3 % of cases (Table 2), which are numbers slightly higher than the perinatal mortality of at least one twin reported in literature which varies from 0,5 to 6,8 % [17,21,22]. However, it is crucial to interpret these findings cautiously, considering our data collection occurred at a tertiary-level center where more complex pregnancies are often referred.

By using the same placental stratification described by Couck *et Al.* (2018) [16], our data align with their classification, which divides patients into three cohorts of patients that have increasing umbilical insertion discordance (concordant, intermediate, or discordant). Prior to their paper, most studies focused only on the presence of one aberrant cord insertion without considering the type of the other twin's insertion. Our findings revealed a significant positive correlation (p = 0.03) exists between birth weight discordance and discordance in twins' umbilical cord insertions' sites. This correlation suggests that birth weight discordance increases alongside umbilical discordance. To our knowledge, this is the first prospective study that reports this result, providing findings consistent with those retrospectively obtained by Couck *et Al.* (2018) [16].

The strong correlation found between the type of umbilical cord insertion and feto-neonatal adverse events also holds significant importance, particularly from a pathophysiological perspective. In addition, it highlights the potential value of early ultrasound assessment of umbilical cord insertion sites in predicting fetal and neonatal adverse events, despite the current lack of widespread recommendations in guidelines. Given our findings, this evaluation, conducted as early as the first or second trimester ultrasound scan, could help identify MC twins at a heightened risk of discordant growth [25]. Our clinical experience

confirms that the best timing to visualize and study cord insertion sites appears to be at the end of the first trimester. Robust prospective studies with larger cohorts are needed to accurately establish this association and evaluate the accuracy of ultrasound in this context. Such investigations could inform the modification of current management protocols and their incorporation into future diagnostic or therapeutic criteria.

Given the observed inverse association between survival rates and birth weight discordance [10], we also explored the hypothesis of a potential correlation between umbilical insertion discordance and adverse neonatal events. However, our analysis did not reveal a significant correlation between these two variables. It's noteworthy that among the group of pregnancies without fetal or neonatal adverse events (n = 25), there were no instances of discordant umbilical cords. In contrast, within the group experiencing at least one adverse event (n = 51), a discordant umbilical cord rate of 13.7 % was observed.

Regarding the presence of anastomoses and the occurrence of CMPO or CNAO, our study did not establish a significant correlation, despite previously reported data (Table 3) [8,11,23].

While this study possesses the strength of prospective data collection from early pregnancy, minimizing the risks of selection bias, we acknowledge several limitations. Data collection occurred at a tertiary referral center, potentially introducing a selection bias towards complicated pregnancies. Additionally, the exclusion of pregnancies complicated by remote fetal demise and the possibility of missing small anastomoses due to incomplete injection are inherent limitations. Lastly, the small sample size of our study does limit its statistical power. We are committed to expanding our cohort to provide a more robust basis for assessing these correlations, offering a clearer understanding.

In conclusion, MC twin pregnancies remain a complex obstetric challenge with a considerable rate of adverse perinatal outcomes [20,24]. It is paramount to correctly identify chorionicity during the first-trimester ultrasound scan. Subsequent management of MC pregnancies should involve a multidisciplinary team in third-level centers experienced in their unique clinical management, emphasizing early recognition and adequate differential diagnosis of MC complications to offer timely interventions when necessary [13]. Our findings suggest that routine first-trimester assessment of umbilical cord insertion sites may be beneficial in predicting perinatal adverse events, particularly for MC twin pregnancies. Further research with larger cohorts is warranted to strengthen these findings and evaluate the utility of ultrasound in this context. By incorporating discordant cord insertions into existing protocols, healthcare providers may enhance risk stratification and resource allocation for the improved management of MC twin pregnancies.

Declaration of competing interest

The authors report no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.placenta.2023.10.007.

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