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## Updates

### Management of monoamniotic twin pregnancies: where, when, how?

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## Updates

### Management of monoamniotic twin pregnancies : where, when, how ?

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#### **Abstract (<250 words)**

Management difficulties for monochorionic monoamniotic (MCMA) twin pregnancy reflect the absence of high-quality research into optimal types of monitoring, essential as MCMA twins have a high risk of intrauterine and neonatal death with perinatal mortality.

D'Antonio et al's meta-analysis and the MonoMono study published in 2019, investigated the impact of monitoring location, out- or in-patient, of MCMA pregnancies and concluded that no specific management location is associated with improvement in prognosis.

To evaluate the optimal timing for delivery of MCMA pregnancies, Van Mieghem and Chitrit carried out retrospective studies comparing gestational age of intrauterine death and risk of neonatal complication. The crossover point between the prospective risk of intrauterine fetal death and neonatal complication was found at 32–33 weeks of gestation (WG), in accordance with American College of Obstetricians and Gynecologists and Royal College of Obstetricians and Gynaecologists recommendations but inclusion of complicated pregnancies and analysis of fetuses individually may be regarded as a bias.

The majority of studies of MCMA pregnancies focused on elective scheduled cesareans, with only rare retrospective studies reporting on vaginal delivery. Of these, two recent studies carried out by French teams suggest that vaginal deliveries may be as safe as cesarean births for MCMA twin pregnancies when specific criteria are met.

In summary, concerning MCMA pregnancies, prognosis is not found to improve with inpatient management, optimal timing for delivery is at approximately 33 GW and vaginal delivery should not be excluded.

**Keywords (<6)** monochorionic monoamniotic twin pregnancy, twin delivery

**Main text**

Management of monochorionic monoamniotic (MCMA) twin pregnancy is challenging. The rare occurrence of MCMA twins is an obstacle for performing quality studies that seek to assess optimal type of monitoring in terms of type and frequency of follow-up and timing or mode of delivery, and to provide specific recommendations for management of these pregnancies. There is also a wide variation in practice among recently published studies with regard to type and frequency of fetal monitoring, and timing of initiation of fetal surveillance. National Institute for Health and Care Excellence (NICE) guidance (England & Wales, 2011) on antenatal management of twin and triplet pregnancies have highlighted the insufficient evidence regarding effective clinical management of MCMA twin pregnancies and the need for further research to inform future NICE guidelines (1). MCMA twins which share an amniotic sac are rarer, occurring in about 3.6-5% of MC pregnancies and in 0.6-1 in 10 000 pregnancies overall (2-4).

MCMA twins are at high risk of intrauterine and neonatal death with perinatal mortality ranging between 10 and 40% (5-10). This high perinatal mortality rate is partially the result of an increased incidence in congenital anomalies (up to 26%)(5) as well as to twin-reversed-arterial-perfusion sequence and conjoined twinning (10). The single placenta and amniotic cavity shared by two fetuses contributes too at the high perinatal risk of mortality. This is invariably associated with umbilical cord entanglement (11,12) and large vascular intertwin anastomoses at placental level (6) leading to cord accidents, acute blood volume shifts from one fetus to the other, and more rarely, twin-twin transfusion syndrome.

MCMA pregnancy complications, as for other twin pregnancies, include preterm delivery. These complications particularly resemble monochorionic twin pregnancies with regard to an increased number of abnormal fetuses (23.3% of MCMA)(13), selective utero growth restriction (sIUGR)(14) and twin-to-twin transfusion syndrome (TTTS)(9-15% of MCMA)(15,16). The most serious specific MCMA pregnancy complication concerns cord knots. Although perinatal mortality of MCMA twins has considerably reduced over the last two decades compared with the extremely high rates of up to 70% reported previously (17), the mortality rate remains relatively high despite improved surveillance and care.

To prevent these complications, monitoring is intensified after fetal viability, the mother-to-be may be required to stay in hospital and delivery is typically proposed from 32 WG by cesarian by anglo saxon guidelines (18,19).

French guidelines published in 2009 (20), recommend monitoring of MCMA twin pregnancies in collaboration with a tertiary hospital. As for monochorionic diamniotic twin pregnancies, ultrasound monitoring with fetal Dopplers, amniotic and bladder evaluation, and cervical length measurement are recommended every two weeks from 16 WG onwards. Increased obstetric monitoring must be observed after 27-30 WG either during inpatient management in a tertiary maternity hospital or on an outpatient basis in partnership with a tertiary hospital. These recommendations stipulate that delivery should be performed from 32 WG and before 36 WG, by cesarian. The vaginal delivery remains acceptable in tertiary centers sensitized to the funicular perpartum risks.

The objectives of this update are to evaluate the interest of maternal hospitalisation monitoring, to discuss the optimal time and the mode of delivery in the MCMA pregnancies. In the first time, we have selected in Medline database, using « monoamniotic » and « management » terms, the publications of the last 5 years, in french or english languages. Among 39 articles, we have excluded editorial, case reports, national guidelines, review and publications concerned specific complications of twin pregnancy (preterm birth, in utero growth restriction (IUGR), TTTS, acardiac twin, chromosomal abnormalities, conjoined twins, triplet pregnancies. Then we have excluded studies including in the most recent meta-analysis, and we obtained 3 articles, the D'antonio et al's meta-analysis (21), the MonoMono multinational cohort study (20) and the Chitrit et al.'s retrospective study (4). To argument the results of Chitrit study, we have researched, in Medline database, the older studies published after 2009 (year of the French guidelines (20)) on the optimal time and the mode of MCMA delivery. So we added two studies: Van Mieghem retrospective study (2014) (13) and Anselem study (2015) (22).

#### The impact of monitoring location:

D'antonio et al's meta-analysis (21) and the MonoMono multinational cohort study (20) considered the impact of monitoring location by comparing in- and outpatient management of MCMA pregnancies (table 1) in several centers and countries. They reported a high level of heterogeneity between the participating centers concerning management and did not comment on type and frequency of follow-up. To evaluate optimal timing of delivery for MCMA pregnancies, Van Mieghem et al. (13) and Chitrit et al. (4) proposed retrospective studies comparing intrauterine fetal deaths (IUFD) and neonatal morbi-mortality risks. Concerning MCMA delivery mode, two recent French publications focused on vaginal delivery (4,22).

The meta-analysis performed by D'Antonio et al. (21) was based on twenty-five studies, with 814 non-anomalous twin pairs reaching 24 GW and described the fetal risks of MCMA pregnancies. Twenty studies reported perinatal outcomes of MCMA pregnancies according to follow-up locations. The perinatal risk was not found to differ according to in- or outpatient management. Most IUFDs were

unexpected, raising questions concerning an optimal type of assessment in these pregnancies (table 1). Approximately 38% (95% CI, 28.0–48.2%) of MCMA pregnancies were delivered before the scheduled time, mainly due to spontaneous preterm labor or abnormal cardiotocographic findings, with no significant difference between in or outpatient management. This meta-analysis did not report on mode of delivery.

The multinational cohort study (23) focused on management of MCMA pregnancies occurring between January 2010 and January 2017, in 22 participating study centers for 195 non-anomalous and uncomplicated MCMA twins from 26 WG. Women managed as inpatients were admitted from 24<sup>+0</sup> to 29<sup>+0</sup> WG until delivery. In inpatient and outpatient groups planned cesarean delivery was scheduled usually at 32<sup>+0</sup> to 34<sup>+6</sup> WG, according to local protocols. 4 centers scheduled cesarean until 34<sup>+6</sup> WG, 1 until 35<sup>+6</sup> WG and 1 until 36<sup>+0</sup> WG. Inpatient and outpatient management policies were highly variable between the included centers. Demographic characteristics were similar between the two groups. Non-anomalous uncomplicated MCMA twin pregnancies managed as inpatients had a similar rate of IUFD to those managed as out-patients (table 1). The highest weekly IUFD rate was observed between 29<sup>+0</sup> and 29<sup>+6</sup> WG, in both the inpatient group (rate, 2.0%) and the outpatient group (rate, 6.0%). From 32<sup>+0</sup> to 36<sup>+0</sup> WG, no fetal or neonatal death occurred in either group. 70.7% of women in the inpatient group and 68.3% of women in the outpatient group delivered via scheduled cesarean section on the planned date.

These studies concluded that the location of MCMA management did not improve the prognosis of these twin pregnancies. However, one of the main biases of this study concerns a high level of heterogeneity in pregnancy management between the participating centers, and subsequent confusion between physical location and surveillance protocol. This was highlighted in Van Mieghem's editorial published in 2019 (24), which also underlined the importance of centers presenting their results with well-described protocols, to allow for more detailed (individual-patient) meta-analysis.

#### The optimal age of delivery:

The study of mortality rates according to gestational age for delivery in D'Antonio et al's meta-analysis(21) and in the MonoMono cohort study(23), found 0-2.2% antenatal mortality after 32 WG, raising the issue of elective very preterm delivery (32 WG)(10). Results regarding optimal timing of elective delivery of MCMA twin pregnancies and the effect of cord entanglement on perinatal outcome are inconsistent. Some studies advocate expectant management after 20 WG, predicting a good prognosis for uncomplicated MCMA twin pregnancies despite the existence of cord entanglement(10,12). Glinianaia SV et al reported that most MCMA pregnancies surviving beyond 24 WG with a clear diagnosis of cord entanglement had good perinatal outcome(3). In order to assess the

optimal timing for delivery of MCMA pregnancies, Van Mieghem et al. (13) and Chitrit et al. (4) have drawn up retrospective studies comparing IUFD and neonatal morbi-mortality risks.

Van Mieghem et al. published a retrospective multicenter cohort study conducted over a 9 year period in eight university hospitals (13) with 193 monoamniotic twin pregnancies (386 fetuses). Fifty-three fetuses in 45 pregnancies (23.3%) were diagnosed with congenital anomalies. Seventy fetuses (18.1%) from 42 pregnancies died during pregnancy, including 7 iatrogenic IUFD for congenital anomalies or TTTS. The results showed that the prospective risk of noniatrogenic IUFD per fetus decreased from 16.3% (61/375) at 11 WG to its lowest point at 1.4% (4/290) at 28 WG, but then increased between 32 and 34 WG to 5.1%. No IUFD were recorded among the 23 pregnancies (18 of which had two live fetuses) that continued beyond 34<sup>+1</sup> WG. The prospective risk of IUFD in MCMA twins outweighed the risk of a non-respiratory neonatal complication at 32<sup>+4</sup> WG, indicating that optimal timing for elective delivery is at approximately 33 WG. The optimal timing of deliveries was evaluated without differentiating between pregnancies with or without foeto-placental anomalies.

Chitrit et al.'s retrospective study covered cases over an extensive period of 26 years, from a single university hospital between January 1992 and March 2018 (4). Timing of delivery of otherwise uncomplicated MCMA twins was scheduled near 36 WG.

46 MCMA twin pregnancies (92 fetuses) were identified during this period (excluding conjoined and acardiac twins). In all, 21 fetuses in 17 pregnancies (37.0%) were diagnosed with congenital malformations. One unexplained IUFD was diagnosed at 36<sup>+5</sup> WG in a pregnant woman managed as an inpatient. The prospective risk of IUFD across the gestational age spectrum rose from 10.0% (9/90) at 13<sup>+2</sup> WG to 11.3% (9/80) at 20 WG. It then reached its lowest level of 1.8% (1/57) at 33<sup>+6</sup> WG and rose again sharply from 34 to 36<sup>+4</sup> WG to 16.7% (1/6). Conversely, the prospective risk of neonatal mortality and morbidity in this population dropped to 0% at 36<sup>+3</sup> WG, despite two interim peaks at 34<sup>+2</sup> (7.7%) and 36<sup>+1</sup> (10.0%) WG. Among the 80 fetuses with neither medically indicated terminations nor major congenital anomalies, the prospective risk of neonatal mortality and morbidity by gestational age decreased sharply after 28 WG. The prospective risk of IUFD by gestational age was lowest at 30 WG, subsequently rising in the period up to 38 WG. The curve for prospective risk of any neonatal complication crossed the curve for prospective risk of IUFD at 33<sup>+1</sup> WG (95% CI 29<sup>+4</sup>–35<sup>+3</sup> WG) at a level of 4.4%. The authors concluded that delivery for uncomplicated MCMA twin pregnancies should be considered at around 33 WG and no later than 35 WG.

The results of these retrospective studies concerning the crossover point between the prospective risk of IUFD and neonatal complication lend support to the recommendations of the American College of Obstetricians and Gynecologists (18) and the Royal College of Obstetricians and Gynaecologists (19) for delivery of MCMA twins at 32–34 WG. These studies attempted to avoid bias related to foeto-placental complications by excluding fetuses with medically indicated terminations or major congenital

anomalies. However, these fetoplacental complications (sIUGR and TTTS) have consequences on the co twin and therefore on the whole pregnancy. The consideration of fetuses individually and not in pairs within the same pregnancy renders difficult transposition of this finding to uncomplicated MCMA pregnancies. Consequently exclusion of pregnancies involving medically indicated terminations or major congenital anomalies and therefore both fetuses, appears necessary for estimation of the optimal age of delivery of uncomplicated MCMA pregnancies.

#### The mode of delivery:

The majority of studies focusing on MCMA pregnancies reported an elective scheduled cesarean. Only rare retrospective studies report the practice of vaginal delivery in MCMA twin pregnancies, the most recent of which were published by French clinicians, in 2015 by the Port-Royal Hospital team (Paris) (22) and in 2020 by the Robert-Debré Hospital team (Paris) (4) (table 2).

The first study (22) reported outcomes of 38 MCMA twin pregnancies managed homogeneously in the single tertiary hospital, between 1993 and 2014, to assess the feasibility of continuing pregnancy beyond 32 WG combined with vaginal delivery. After exclusion of pregnancies with fetal malformations, the overall rate of IUFD among all 70 fetuses was 8.6%. Mean gestational age at delivery was 33.8 WG (range 25.6–36.3). 26 women (78.8%) gave birth at or after 32 WG, and among these women, 24 women gave birth after 34 WG. No IUFD or neonatal deaths occurred after 32 WG. At or after 32 WG, vaginal birth was planned for 21 women (80.8%), of whom 17 underwent induction of labour (65.4%). Finally, 14 women had vaginal deliveries and 12 had cesarean sections (53.8 and 46.2%, respectively). Labour was induced in 12 of the 14 women who had vaginal deliveries. Two women had operative deliveries. Neonatal outcomes were similar whatever the mode of delivery. No difficulties or complications related to vaginal deliveries were reported.

In the Chitrit study (4), the timing of delivery of otherwise uncomplicated MCMA twins was scheduled near 36 WG. Mode of delivery was decided during daily obstetric staff meetings. Among 46 MCMA twin pregnancies (92 fetuses), 41 were delivered at or after 23 GW. 37 women gave birth to 64 live infants at median gestational age of 35.0 (IQR 1.9) GW. Delivery was by cesarean section in 17 (45.9%) of these 37 pregnancies and 19 (51.4%) women delivered vaginally. In one pregnancy (2.7%), the first twin was delivered vaginally and the second by cesarean section. Gestational age at delivery was not significantly different ( $p = 0.849$ ) between women with vaginal deliveries (median value 35.0, IQR 1.7) and those with cesarean deliveries (median value 35.1, IQR 3.8). Neonatal outcomes did not differ according the mode of delivery. Moreover 28 women, with both twins alive at the onset of labor, gave birth at 23 GW or later. Fourteen (50.0%) were delivered by cesarean section and 13 (46.4%) vaginally.



Similarly, neonatal outcomes did not differ significantly between the 27 infants born vaginally and the 29 born by caesarean section.

These observational studies suggest that vaginal deliveries may be as safe as cesarean births for MCMA twin pregnancies when specific criteria are met, first twin in cephalic presentation, no uterine scar and estimated weight difference between the twins less of 30% (22).

In conclusion, MCMA pregnancy prognosis was not found to improve with inpatient management after 24 WG. Further studies focusing on frequency and methods of MCMA monitoring are required to establish an optimal surveillance protocol. Studies concerned the evaluation of an optimal age for MCMA delivery agree on 32-33 WG, in accordance with current guidelines (23,24) although the inclusion of complicated pregnancies and the consideration of fetuses individually could be considered as a bias. However, the low rate of fetal loss occurring after 32 WG and the persistence of risk of complications related to prematurity at this term may lead to continuing the pregnancy after 34 WG due to the absence of intercurrent complications. Some retrospective studies suggested that when specific criteria are met, vaginal deliveries are safe in MCMA pregnancies in centers with a great expertise of vaginal delivery with multiples pregnancies and after accurate information because of funicular risks.

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		D'antonio et al (13)		MonoMono study (20)		Van Mieghem et al (14)		Chitrit et al (4)		Anselem et al (21)										
		Fetuses (n/N)	Pooled proportions (95% CI) (%)	Fetuses		Fetuses		Fetuses		Fetuses										
				(n/N)	(%)	(n/N)	(%)	(n/N)	(%)	(n/N)	(%)									
Overall mortality	Overall IUFD	106/1628	5.8 (4.0-8.1)	31/390	7.9	11/306	3.6	27/92	29.3	11/76	14.5									
	siIUFD	38/1628	2.5 (1.8-3.3)	7/390	1.8	Not specified		11/92	12.0	3/76	3.9									
	diIUFD	68/1628	3.8 (2.5-5.3)	24/390	6.2	Not specified		16/92	17.4	8/76	10.5									
	NND	37/1628	2.6 (1.9-3.4)	11/390	2.8	17/306	5.6	2/92	2.2	0/76	0									
	PND	143/1628	7.9 (5.9-10.2)	42/390	10.8	Not specified		28/92	30.4	0/76	0									
Perinatal mortality according the antenatal management	Inpatient	Overall IUFD	19/610	3.0 (1.4-5.2)	5/150	3.3	2/142*	14.1	Not specified		Not specified									
		siIUFD	9/610	1.9 (0.9-3.1)	Not specified		0/142 *	0												
		diIUFD	10/610	1.6 (0.5-3.3)	Not specified		2/142 *	14.1												
		NND	8/610	1.5 (0.7-2.6)	1/150	0.7	Not specified													
		PND	27/610	3.7 (1.5-6.9)	6/150	4.0	Not specified													
	Outpatient	Overall IUFD	67/830	7.4 (4.4-11.1)	26/240	10.8	5/106 *	4.7												
		siIUFD	17/830	2.9 (1.2-4.0)	Not specified		1/106 *	0.9												
		diIUFD	50/830	5.3 (3.2-8.0)	Not specified		4/106 *	3.8												
		NND	21/830	2.7 (1.6-3.9)	10/240	4.2	Not specified													
		PND	88/830	9.5 (5.9-13.9)	36/240	15.0	Not specified													
		Before 30 GW included		Overall IUFD (≥24WG)	84/1628	4.3 (2.5-6.2)	29/390 (≥27WG)	7.4					3/306 (≥23WG)	1.0	Described with regression line figure		11/76	14.5		
				siIUFD (≥24WG)	30/1628	2.0 (1.4-2.7)	7/390 (≥27WG)	1.8					1/306 (≥23WG)	0.3			Not specified			
		diIUFD (≥24WG)	54/1628	2.9 (1.8-4.2)	22/390 (≥27G)	5.6	2/306 (≥23WG)	0.7	Not specified											
		NND (≥24WG)	35/1628	2.5 (1.8-3.3)	Not specified		4/306 (≥23WG)	1.3	3/76	3.9										
		PND (≥24WG)	119/1628	6.2 (4.4-8.3)	Not specified		7/306 (≥23WG)	2.3	14/76	18.4										
31-32 GW		Overall IUFD	11/1266	1.0 (0.6-1.7)	2/278	0.7	Described with regression line figure		Described with regression line figure		0/54	0								
		siIUFD	5/1266	0.6 (0.2-1.1)	0/278	0					0/54	0								
		diIUFD	6/1266	0.7 (0.3-1.2)	2/278	0.7					0/54	0								
		NND	2/1266	0.6 (0.2-1.1)							0/54	0								
		PND	13/1266	1.3 (0.7-2.0)							0/54	0								
33-34 GW		Overall IUFD	11/606	2.2 (0.9-3.9)	0/134	0					Described with regression line figure		Described with regression line figure				0/46	0		
		siIUFD	3/606	1.0 (0.4-1.9)	0/134	0											0/46	0		
		diIUFD	8/606	1.6 (0.6-3.0)	0/134	0									0/46	0				
		NND	0/606	0 (0-1.4)	Not specified										0/46	0				
		PND	11/606	2.2 (0.9-3.9)	Not specified												0/46	0		
35-36 GW		Overall IUFD	0/150	0 (0-4.0)	0/120	0									Described with regression line figure		Described with regression line figure		0/40	0
		siIUFD	0/150	0 (0-4.0)	0/120	0													0/40	0
		diIUFD	0/150	0 (0-4.0)	0/120	0	0/40	0												
		NND	0/150	0 (0-4.0)	Not specified		0/40	0												
		PND	0/150	0 (0-4.0)	Not specified				0/40	0										
Mode of delivery	Cesarean	Not specified		270/390	69.2	296/306	96.7	36/76	47.4	36/76									47.4	
	Vaginal delivery			120/390	30.8	10/306	3.3	40/76	52.6	40/76									52.6	

\* after 26 WG without fetal or obstetric complication

WG : week of gestation ; IUFD : intrauterine fetal death ; NND : neonatal death ; PND : perinatal death

Table 1 : Perinatal mortality and mode of delivery of MCMA pregnancies according studies

	Anselem et al. (21)			Chitrit et al. (4)		
	50 neonates from the 26 women who gave birth at or after 32 WG			64 neonates from the 37 women who gave birth at or after 23 WG		
	Caesarean section	Vaginal delivery	P	Caesarean section	Vaginal delivery	p
Babies (n (%))	22 (44.0)	28 (56.0)		33 (51.6)	31 (48.4)	
Median pH (range or $\pm$ SD)	7.13 (7.12-7.40)	7.29 (7.15-7.47)	0.62	7.32 ( $\pm$ 0.03)	7.33 ( $\pm$ 0.08)	0.573
pH<7.10 (n (%))	0 (0)	0 (0)	NS	0 (0)	3 (9.7)	0.238
Median at 5-min Apgar (range or $\pm$ SD)	9 (2-10)	9 (5-10)	0.82	10 ( $\pm$ 0)	10 ( $\pm$ 0)	0.573
5-min Apgar < 7 (n (%))	1 (4.5)	1 (3.6)	NS	0 (0)	2 (6.7)	0.223
Hospitalization in NICU (n (%))	15 (68.2)	14 (50.0)	0.25	3 (9.1)	6 (19.4)	0.296
Length of NICU stay (days (range or $\pm$ SD))	6 (2-15)	7 (1-30)	0.21	2.67 ( $\pm$ 1.53)	21.7 ( $\pm$ 23.6)	0.106
Neonatal deaths (n)	0	0	NS			
Composite neonatal complications (n (%))				2 (6.1)	6 (19.4)	0.142

WG : weeks of gestation ; MCMA : monochorionic monoamniotic ; min : minutes ; NICU : neonatal intensive care unit ; SD : standard deviation

Table 2 : Delivery mode of MCMA pregnancy