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Inpatient *vs* outpatient management and timing of delivery of uncomplicated monochorionic monoamniotic twin pregnancy: the MONOMONO study

The MONOMONO Working Group#

KEYWORDS: Cesarean delivery; chorionicity; cord accident; cord entanglement; healthcare; monochorionic; multiple gestation; perinatal death; respiratory distress syndrome; twin pregnancy

ABSTRACT

Objectives *Monoamniotic twin pregnancies are at increased risk of perinatal complications, primarily owing to the risk of cord entanglement. There is no recommendation on whether such pregnancies should be managed in hospital or can be safely managed in an outpatient setting, and the timing of planned delivery is also a subject of debate. The aim of this study was to compare the perinatal outcomes of inpatient* vs *outpatient fetal surveillance approaches employed among 22 participating study centers, and to calculate the fetal and neonatal death rates according to gestational age, in non-anomalous monoamniotic twins from 26 weeks' gestation.*

Methods *The MONOMONO study was a multinational cohort study of consecutive women with monochorionic monoamniotic twin pregnancies, who were referred to 22 university hospitals in Italy, the USA, the UK and Spain, from January 2010 to January 2017. Only non-anomalous uncomplicated monoamniotic twin pregnancies with two live fetuses at 26 + 0 weeks' gestation were included in the study. In 10 of the centers, monoamniotic twins were managed routinely as inpatients, whereas in the other 12 centers they were managed routinely as outpatients. The primary outcome was intrauterine fetal death. We also planned to assess fetal and neonatal death rates according to gestational age per 1-week interval. Outcomes are presented as odds ratio (OR) with 95% CIs. The main outcome was analyzed using both standard logistic regression analysis, in which each fetus was treated as an independent unit, and a generalized mixed-model approach, with each twin pair treated as a cluster unit, considering that the outcome for a twin is not independent of that of its cotwin.*

Results *195 consecutive pregnant women with a non-anomalous uncomplicated monoamniotic twin gestation (390 fetuses) were included. Of these, 75 (38.5%) were managed as inpatients and 120 (61.5%) as outpatients. The overall perinatal loss rate was 10.8% (42/390) with a peak fetal death rate of 4.3% (15/348) occurring at 29 weeks' gestation. There was no significant difference in mean gestational age at delivery (31 weeks), birth weight (~1.6 kg), or emergency delivery rate between the inpatient and outpatient surveillance groups. Based on generalized mixed-model analysis, there was no statistically significant difference in fetal death rates between inpatient management commencing from around 26 weeks compared with outpatient surveillance protocols from 30 weeks (3.3%* vs *10.8%; adjusted OR 0.21 (95% CI, 0.04–1.17)). Maternal length of stay in the hospital was 42.1 days in the inpatient group, and 7.4 days in the outpatient group (mean difference 34.70 days (95% CI, 31.36–38.04 days). From 32 + 0 to 36 + 6 weeks, no fetal or neonatal death in either group was recorded. 46 fetuses were delivered after 34 + 0 weeks, and none of them died* in utero *or within the first 28 days postpartum.*

Conclusion *In uncomplicated monoamniotic twins, inpatient surveillance is associated with similar fetal mortality as outpatient management. After 31 + 6 weeks, and up to 36 + 6 weeks, there were no intrauterine fetal deaths or neonatal deaths. Copyright © 2018 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

Monochorionic monoamniotic twinning accounts for about 1–2% of monozygotic twin pregnancies worldwide[1–6]. Monoamniotic twins are at increased risk of perinatal complications compared with monochorionic

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diamniotic or dichorionic twin pregnancies[3–5]. Perinatal mortality is reported to be high in monoamniotic twins, primarily owing to cord entanglement[5]. Early- and mid-pregnancy loss before 26 weeks' gestation seems to be correlated mainly with the incidence of twin reversed arterial perfusion (TRAP) sequence, conjoined twins and major congenital anomalies, the rate of these complications being as high as 60% in studies evaluating high-risk referred populations[5,7]. Regarding pregnancy loss after 26 weeks, the largest review of monoamniotic twins, including 60 studies and 133 non-conjoined monoamniotic twin pregnancies, reported a non-anomalous perinatal mortality rate of about 20%, with a significant rise in mortality after 32 weeks' gestation[4]. These data are often used to justify planned preterm delivery from 32 weeks in otherwise uncomplicated monoamniotic twins[5,8]; however, robust data on which a decision about the timing of delivery can be based are missing.

Inpatient management of monoamniotic twin pregnancies from viability until delivery has been reported[5]. No recommendation has been made on whether these women should be managed in hospital or whether they can be managed safely in an outpatient setting, and The American College of Obstetricians and Gynecologists (ACOG) concluded that 'the optimal management of these patients remains uncertain'[8].

The aim of this study was to compare the perinatal outcomes of inpatient *vs* outpatient fetal surveillance approaches employed in 22 participating study centers, and to calculate the fetal and neonatal death rate according to gestational age, in non-anomalous monoamniotic twins at $\geq$ 26 weeks' gestation.

SUBJECTS AND METHODS

Study design and participants

This was a multinational, retrospective, cohort study of pregnant women with a monochorionic monoamniotic twin pregnancy who were referred to 22 university hospitals in Italy, the USA, the UK and Spain (Table 1) between January 2010 and January 2017. Clinical records were collected in a dedicated merged database. Only women with a confirmed diagnosis of monoamnionicity after delivery were included.

All reported variables were collected for all the subjects included in the study. Inclusion criteria were gestational age of at least 26 + 0 weeks with both fetuses alive, and confirmation of monoamnionicity at delivery and/or by pathologic examination of the placenta. Only uncomplicated monoamniotic twin pregnancies were included. Exclusion criteria were pseudomonoamnionicity (iatrogenic creation of a single amniotic space because of an invasive procedure); conjoined twins; major fetal abnormality; intrauterine growth restriction (IUGR) or selective IUGR (i.e. one or both fetuses with ultrasound-estimated fetal weight < 10th centile); twin-to-twin transfusion syndrome; TRAP sequence; acardiac twins; spontaneous miscarriage before 26 weeks; and higher-order multiple pregnancies. Women who underwent selective reduction were also excluded. Therefore, all women included in the study had a non-anomalous uncomplicated monoamniotic twin pregnancy with both fetuses alive at 26 weeks.

In 10 of the centers, all monoamniotic twins were managed routinely as inpatients, while in the other 12 centers all monoamniotic twins were managed routinely as outpatients (Table 1). In outpatient care, frequent follow-up was employed, with regular evaluation of fetal wellbeing by ultrasound assessment of fetal growth (fetal biometry of both twins and amniotic fluid volume assessment using deepest vertical pocket) every 3 weeks, ultrasound Doppler (umbilical artery Doppler and middle cerebral artery peak systolic velocity for both twins) every 2 weeks[9], and non-stress tests (NST) usually once a week with either standard NST or computerized cardiotocography.

Women managed as inpatients were admitted from 24 + 0 to 29 + 0 weeks until delivery. Patient management in this group included NST two or three times a day, ultrasound assessment of fetal growth every 3 weeks and Doppler ultrasound every 2 weeks (Table 1)[9]. Continuous fetal heart rate monitoring was not performed in any of the participating centers.

All women in the inpatient group (study group) were delivered following one admission. For women included in the outpatient group (comparison group), who had one or more admissions, the total length of stay was calculated.

In both groups, planned Cesarean delivery was scheduled usually at 32 + 0 to 34 + 6 weeks, according to local protocols and at the provider's discretion (Table 1)[8,10]. Any indication for earlier delivery was recorded. Antenatal corticosteroids for fetal lung maturation were offered before planned Cesarean delivery. Assessment of cervical length by transvaginal ultrasound for the prevention of preterm birth was not performed routinely in either group, given the lack of treatment for twin pregnancies with a short cervix[11–16].

Outcomes

Primary and secondary outcomes were compared between the inpatient and outpatient groups. The primary outcome was intrauterine fetal death (i.e. stillbirth) after 26 weeks' gestation. Secondary outcomes were gestational age at delivery, total antenatal maternal length of stay (LOS) in the hospital, indication for delivery, birth weight, LOS in the neonatal intensive care unit (NICU) (days from admission to the NICU until discharge), neonatal death (i.e. death of a liveborn baby within the first 28 days postpartum) and perinatal death (i.e. either fetal or neonatal death).

We also planned to assess fetal and neonatal death rates according to gestational age at 1-week intervals; this secondary analysis was performed separately for the inpatient and outpatient groups.

Table 1 Protocol followed in participating centers for inpatient or outpatient management of uncomplicated monochorionic monoamniotic twin pregnancy with two live fetuses at 26 weeks' gestation

Center	*Protocol*	*Planned Cesarean delivery (weeks)*
Outpatient management		
University of Naples Federico II, Naples, Italy	US fetal growth every 3 weeks; US Doppler every 2 weeks; CCTG once a week starting from 30 + 0 weeks	32 + 0 to 34 + 6
Careggi Hospital University of Florence, Florence, Italy	US fetal growth every 2 weeks; US Doppler every 1 week; only one CCTG on day before planned Cesarean delivery	32 + 0 to 33 + 6
University of Chieti, Chieti, Italy	US fetal growth every 3 weeks; US Doppler every 2 weeks; CCTG once a week starting from 30 + 0 weeks	32 + 0 to 33 + 6
University of Padua, Padua, Italy	US fetal growth every 3 weeks; US Doppler every 2 weeks; CCTG once a week starting from 30 + 0 weeks	32 + 0 to 35 + 6
University of Udine, Udine, Italy	US fetal growth every 3 weeks; US Doppler every 2 weeks; CCTG once a week starting from 30 + 0 weeks	32 + 0 to 33 + 6
Magna Graecia University of Catanzaro, Catanzaro, Italy	US fetal growth every 4 weeks; US Doppler every 2 weeks; CCTG once a week starting from 30 + 0 weeks	33 + 0 to 36 + 6
University Tor Vergata, Rome, Italy	US fetal growth every 3 weeks; US Doppler every 2 weeks; CCTG once a week starting from 30 + 0 weeks	32 + 0 to 32 + 6
University of Sapienza, Rome, Italy	US fetal growth every 3 weeks; US Doppler every 2 weeks; CCTG once a week starting from 30 + 0 weeks	33 + 0 to 33 + 6
Buzzi Children's Hospital, Milan, Italy	US fetal growth and US Doppler every 2 weeks between 16 and 24 weeks, then weekly	32 + 0 to 32 + 6
Hospital General Universitario de Ciudad Real, Ciudad Real, Spain	US fetal growth every 3 weeks; US Doppler every 2 weeks; only one CCTG on day before planned Cesarean delivery	32 + 0 to 32 + 6
Hospital General Universitario Gregorio Maranon, Madrid, Spain	US fetal growth every 3 weeks; US Doppler every 2 weeks; CCTG once a week starting from 30 + 0 weeks	33 + 0 to 34 + 6
University College London Hospitals (UCLH), London, UK	US fetal growth every 2 weeks; US Doppler every 2 weeks; CCTG once a week starting from 30 + 0 weeks	32 + 0 to 35 + 0
Inpatient management		
Treviso Hospital, Treviso, Italy	Admission between 27 + 0 and 27 + 6 weeks; US fetal growth every 2 weeks; US Doppler every week; CCTG once or twice a day	32 + 0 to 32 + 6
St Orsola Malpighi Hospital, University of Bologna, Bologna, Italy	Admission between 27 + 0 and 27 + 6 weeks; US fetal growth every 2 weeks; US Doppler every week; CCTG once or twice a day	32 + 0 to 33 + 6
University of Parma, Parma, Italy	Admission between 24 + 0 and 24 + 6 weeks; US fetal growth every 2 weeks; US Doppler twice a week; NST twice a day	32 + 0 to 32 + 6
University of Brescia, Brescia, Italy	Admission between 28 + 0 and 28 + 6 weeks; US fetal growth every 2 weeks; US Doppler every week; CCTG twice a day	32 + 0 to 32 + 6
University of Turin, Turin, Italy	Admission between 28 + 0 and 29 + 0 weeks; US fetal growth every 2 weeks; US Doppler twice a week; CCTG two or three times a day	32 + 0 to 33 + 0
Thomas Jefferson University, Philadelphia, PA, USA	Admission between 26 + 0 and 27 + 6 weeks; US fetal growth every 3 weeks; US Doppler every 2 weeks; NST three times a day	32 + 0 to 33 + 0
The Johns Hopkins Hospital, Baltimore, MD, USA	Admission between 26 + 0 and 27 + 6 weeks; US fetal growth every 3 weeks; US Doppler every 2 weeks; NST three times a day	32 + 0 to 33 + 0
University of Massachusetts-Baystate, Springfield, MA, USA	Admission between 26 + 0 and 27 + 6 weeks; US fetal growth every 3 weeks; US Doppler every 2 weeks; NST three times a day	32 + 0 to 32 + 6
Baylor College of Medicine, Houston, TX, USA	Admission between 26 + 0 and 27 + 6 weeks; US fetal growth every 3 weeks; US Doppler every 2 weeks; NST three times a day	32 + 0 to 34 + 6
Hospital Universitario Central de Asturias (HUCA), Oviedo, Spain	Admission between 27 + 0 and 27 + 6 weeks; US fetal growth every 2 weeks; US Doppler every 2 weeks; NST twice a day	32 + 0 to 34 + 6

Ultrasound (US) assessment of fetal growth included fetal biometry of both twins and amniotic fluid volume assessment using deepest vertical pocket method. US Doppler assessment included umbilical artery Doppler and middle cerebral artery peak systolic velocity assessment, in both twins. CCTG, computerized cardiotocography; NST, non-stress test.

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) v. 19.0 (IBM Inc., Armonk, NY, USA). Data are shown as mean ± SD, median (range) or *n* (%). Univariate comparisons of dichotomous data were performed using the chi-square test with continuity correction. Comparisons between groups were performed using the *t*-test to test means with SD by assuming equal within-group variance, and the Mann–Whitney *U*-test to test group medians with range. Primary and secondary outcomes are presented as odds ratios (ORs) with 95% CIs[17]. In addition to standard logistic regression analysis, in which each fetus was treated as an independent unit, we used a generalized mixed-model approach in which each twin pair was a cluster unit. This model was used because the outcome of a twin is not independent of that of its cotwin. Two-sided *P*-values were calculated, and $P < 0.05$ was considered to indicate statistical significance[18]. The study was reported following the STROBE guidelines[19].

RESULTS

In total, 195 consecutive women with a non-anomalous uncomplicated monoamniotic twin pregnancy (390 fetuses) and both fetuses alive at 26 weeks, were included in the study (Figure 1). Of these, 75 (38.5%) women were managed as inpatients and 120 (61.5%) as outpatients. Inpatient and outpatient management policies were highly variable between the included centers. Inpatient monitoring usually started at about 26 weeks' gestation, whereas in the outpatient group monitoring was usually instituted after 30 weeks (Table 1). Demographic characteristics were similar between the two groups (Table 2). Mean maternal age was about 30 years in both groups. One woman in the inpatient group and one in the outpatient group had a history of stillbirth in a prior pregnancy.

Primary analysis

Based on standard logistic regression analysis, non-anomalous uncomplicated monoamniotic twin pregnancies managed as inpatients from 26 weeks to delivery had a significantly lower rate of intrauterine fetal death (3.3% *vs* 10.8%; OR, 0.28 (95% CI, 0.11–0.76)) and perinatal death (4.0% *vs* 15.0%; OR, 0.24 (95% CI, 0.10–0.58)), and shorter length of NICU stay by approximately 16 days (mean difference (MD) −15.90 days (95% CI, −23.6 to −8.25 days)), compared with pregnancies managed as outpatient. Mean maternal LOS in the hospital was 42.1 days in the inpatient group and 7.4 days in the outpatient group (MD, 34.70 days (95% CI, 31.36–38.04 days)) (Table 3).

However, based on generalized mixed-model analysis considering each twin pair as a cluster unit, non-anomalous uncomplicated monoamniotic twin pregnancies managed as inpatient had a similar rate of intrauterine fetal death as did those managed as outpatient (raw rates: 3.3% *vs* 10.8%; adjusted OR, 0.21 (95% CI, 0.04–1.17); Table 4).

Indications for delivery are shown in Table 5. 70.7% of the women in the inpatient group and 68.3% of the women in the outpatient group delivered via scheduled Cesarean section on the planned date.

Secondary analysis

The overall fetal, neonatal and perinatal death rates in our cohort were 7.9% (31/390), 2.8% (11/390) and 10.8% (42/390), respectively. Four (5.3%) women in the inpatient group and 15 (12.5%) in the outpatient group experienced intrauterine fetal death. Details of fetal, neonatal and perinatal deaths according to gestational age at delivery are shown in Tables 6, S1 and S2, respectively.

The intrauterine fetal death rate per 1-week gestational-age interval ranged from 0% to 4.3%. The highest weekly intrauterine fetal death rate was observed between 29 + 0 and 29 + 6 weeks, in both the inpatient group (rate, 2.0%) and the outpatient group (rate, 6.0%).

From 32 + 0 to 36 + 6 weeks, no fetal or neonatal death occurred in either group (Tables 6 and S1), with 0/46 perinatal deaths between 34 + 0 and 34 + 6 weeks, 0/20 between 35 + 0 and 35 + 6 weeks and 0/10 between 36 + 0 and 36 + 6 weeks (Table S2).

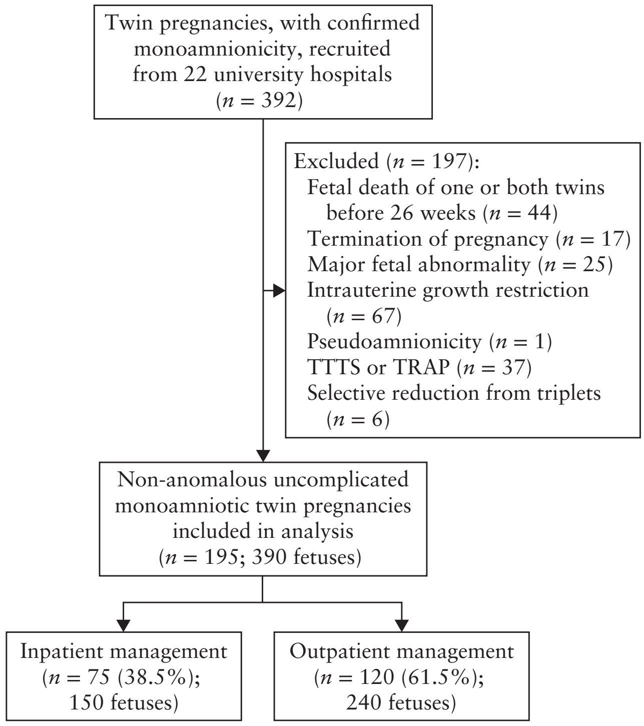

Figure 1 Flowchart showing inclusion in study of uncomplicated monochorionic monoamniotic twin pregnancies with two live fetuses at 26 weeks' gestation. TRAP, twin reversed arterial perfusion; TTTS, twin–twin transfusion syndrome.

Table 2 Baseline characteristics of 195 women with uncomplicated monochorionic monoamniotic twin pregnancy with two live fetuses at 26 weeks' gestation, according to whether they were managed as inpatients or outpatients

Characteristic	*Inpatient management (n = 75)*	*Outpatient management (n = 120)*	P
Age (years)	28.8 ± 5.5	30.0 ± 4.3	0.12
Assisted reproductive technology	5 (6.7)	10 (8.3)	0.88
Body mass index (kg/m^2)	25.5 ± 5.3	26.2 ± 5.5	0.40
Smoker during pregnancy	9 (12.0)	11 (9.2)	0.71
Ethnicity			0.12
White	59 (78.7)	107 (89.2)	
African-American	6 (8.0)	6 (5.0)	
Other*	10 (13.3)	7 (5.8)	
Gravidity	2 (1–8)	2 (1–7)	0.54
Parity	1 (0–4)	1.5 (0–4)	0.77
Prior stillbirth	1 (1.3)	1 (0.8)	0.99

Data are presented as mean ± SD, *n* (%) or median (range). *Includes Asian and Hispanic.

Table 3 Maternal, fetal and neonatal outcomes of 195 uncomplicated monochorionic monoamniotic twin pregnancies with two live fetuses at 26 weeks' gestation, according to whether they were managed as inpatients or outpatients

Variable	*Inpatient management*	*Outpatient management*	*Mean difference (95% CI)*	*OR (95% CI)*	P*
Maternal outcomes					
Number of women	75	120			
Gestational age at delivery (weeks)	31.6 ± 1.7	31.5 ± 2.4	−0.10 (−0.48 to 0.68)	—	0.64
Maternal LOS in hospital (days)	42.1 ± 14.5	7.4 ± 3.4	34.70 (31.36 to 38.04)	—	< 0.01
Fetal and neonatal outcomes					
Number of fetuses	150	240			
Intrauterine fetal death	5 (3.3)	26 (10.8)	—	0.28 (0.11 to 0.76)	0.01
Neonatal death	1 (0.7)	10 (4.2)	—	0.15 (0.02 to 1.22)	0.08
Perinatal death	6 (4.0)	36 (15.0)	—	0.24 (0.10 to 0.58)	< 0.01
Neonatal outcomes based on liveborn babies only					
Number of liveborn neonates	145	214			
Birth weight (g)†	1646 ± 343	1616 ± 411	30.00 (−48.42 to 108.42)	—	0.45
LOS in NICU (days)†	24.3 ± 18.4	40.2 ± 52.5	−15.90 (−23.55 to −8.25)	—	< 0.01
Neonatal mortality†	1 (0.7)	10 (4.2)	—	0.15 (0.02 to 1.22)	0.08

Data are presented as *n*, mean ± SD or *n* (%). *Standard logistic regression analysis, in which each fetus was treated as an independent unit. †Outcomes based on liveborn babies only. LOS, length of stay; NICU, neonatal intensive care unit; OR, odds ratio.

Table 4 Potential predictors of intrauterine fetal death in uncomplicated monochorionic monoamniotic twin pregnancies with two live fetuses at 26 weeks' gestation

Predictor	*OR (95% CI)*	P*
Inpatient *vs* outpatient management	0.21 (0.04–1.17)	0.07
Gestational age, 1-week increase	0.55 (0.36–0.89)	0.006
Birth-weight discordance, 1% increase	1.03 (0.93–1.14)	0.6

*Generalized mixed-model analysis, treating twin pair as cluster unit. OR, odds ratio.

DISCUSSION

Main findings

In addition to the general risks of monochorionicity and twin pregnancy, monoamniotic twins are at greatly increased risk of neonatal death owing to umbilical cord entanglement. In the past, these risks have been associated with a loss rate as high as 70%[5,13–20]. In this cohort of 390 uncomplicated monoamniotic fetuses, the overall rate of perinatal death was 10.8%.

Based on standard logistic regression analysis, in which each fetus was treated as an independent unit, the rate of intrauterine fetal death was significantly lower in the women managed as inpatients than in those managed as outpatients. We also observed an improvement in neonatal outcomes, with inpatient management associated with a shorter LOS in the NICU. However, using generalized mixed-model analysis, with each twin pair treated as a cluster unit, the rate of intrauterine fetal death was similar between inpatient- and outpatient-management groups. Therefore, our study shows that when treating each fetal death as an independent event, there appears to be a statistically significant difference between inpatient and outpatient groups. However, because second twins have an increased risk of fetal death after the death of a first twin, this finding did not reach statistical difference when twin pairs were analyzed as a cluster unit.

Inpatient monitoring usually started at about 26 weeks' gestation, whereas monitoring was delayed until 30 weeks in the outpatient group. Our study showed that the difference in fetal mortality between the inpatient and the outpatient groups mainly occurred in the 26–30-week window, and that once monitoring has been instituted (be it in the inpatient or in the outpatient group) survival of monoamniotic twins is excellent, and outcomes of inpatient and outpatient groups are similar. Therefore, this study shows clearly that close monitoring is needed to achieve good outcomes in monoamniotic pregnancies, regardless of the surveillance setting.

An important finding of this study is the markedly improved perinatal survival compared with that reported in older literature. This could be explained by improvements in the diagnosis and treatment of monoamniotic twin pregnancies but also by the fact that most losses in these pregnancies are attributable to fetal abnormalities and spontaneous early miscarriage[5], which were excluded from our study. Therefore, these data may truly represent the natural history of non-anomalous uncomplicated monoamniotic twins once viability has been reached.

Our secondary analysis also showed that fetal death in non-anomalous uncomplicated monoamniotic twins occurred up to 31 + 6 weeks. Indeed, the major important and novel finding of the MONOMONO study was the lack of 'late-gestational-age' deaths, suggesting that putting back the planned timing of delivery from 32 to 34 + 6 weeks may be a safe approach for pregnant women with an uncomplicated monoamniotic twin pregnancy. However, while no deaths occurred after 34 weeks, only 23 pregnancies continued beyond this gestation, hence the study was underpowered to draw conclusions on the optimal timing of delivery to avoid stillbirth.

Table 5 Indication for delivery by Cesarean section in 195 uncomplicated monochorionic monoamniotic twin pregnancies with two live fetuses at 26 weeks' gestation, according to whether they were managed as inpatients or outpatients

Indication for delivery	*Inpatient management* (n = 75)	*Outpatient management* (n = 120)	*OR (95% CI)*	P
Maternal	1 (1.3)*	6 (5.0)†	0.26 (0.03–2.18)	0.21
Fetal	11 (14.7)	8 (6.7)	2.41 (0.92–6.29)	0.07
Planned delivery	53 (70.7)	82 (68.3)	1.12 (0.60–2.09)	0.73
Spontaneous onset of labor before planned delivery	10 (13.3)	24 (20.0)	0.62 (0.28–1.37)	0.24

Data are presented as *n* (%). *One case of pre-eclampsia. †Four cases of pre-eclampsia; two cases of placental abruption. OR, odds ratio.

Table 6 Incidence of intrauterine fetal death in 195 uncomplicated monochorionic monoamniotic twin pregnancies ($n = 390$ fetuses) with two live fetuses at 26 weeks' gestation, according to whether they were managed as inpatients or outpatients, by 1-week gestational-age intervals

Gestational age (weeks)	*Total cohort* (n = 390 *fetuses*) n/N *(%)**	*Inpatient management* (n = 150 *fetuses*)		*Outpatient management* (n = 240 *fetuses*)	
		n/N *(%)**	*Details*	n/N *(%)**	*Details*
27 + 0 to 27 + 6	5/390 (1.3)	1/150 (0.7)	1 single death	4/240 (1.7)	2 double deaths
28 + 0 to 28 + 6	6/368 (1.6)	0/148 (0)	—	6/220 (2.7)	2 double deaths; 2 single deaths
29 + 0 to 29 + 6	15/348 (4.3)	3/148 (2.0)	1 single death; 1 double death	12/200 (6.0)	5 double deaths; 2 single deaths
30 + 0 to 30 + 6	3/299 (1.0)	1/135 (0.7)	1 single death	2/164 (1.2)	1 double death
31 + 0 to 31 + 6	2/278 (0.7)	0/120 (0)	—	2/158 (1.3)	1 double death
32 + 0 to 32 + 6	0/240 (0)	0/100 (0)	—	0/140 (0)	—
33 + 0 to 33 + 6	0/134 (0)	0/34 (0)	—	0/100 (0)	—
34 + 0 to 34 + 6	0/46 (0)	0/10 (0)	—	0/36 (0)	—
35 + 0 to 35 + 6	0/20 (0)	0/0 (0)	—	0/20 (0)	—
36 + 0 to 36 + 6	0/10 (0)	0/0 (0)	—	0/10 (0)	—
Overall	31/390 (7.9)	5/150 (3.3)	3 single deaths; 1 double death	26/240 (10.8)	4 single deaths; 11 double deaths

*Denominator is total number of live fetuses at that gestational age, i.e. excluding fetal deaths and delivered babies. OR, odds ratio.

The most important limitation of our study was the retrospective non-randomized approach. Owing to the retrospective nature of the study, it was not possible to separate the importance of hospitalization *vs* the increased frequency of testing *per se*. Because this was not a randomized comparison, the findings were subject to bias. Moreover, since continuous fetal heart rate monitoring was not performed in any of the institutions following inpatient management, it was not possible to assess whether such a monitoring approach could further decrease the rate of fetal death. Inpatient and outpatient management were highly dissimilar between the included centers (Table 1), and therefore variations in management among the different institutions could have influenced our findings. Data on patient satisfaction, neonatal outcomes and economic implications were not available.

Comparison with the literature and implications

Several small studies evaluating perinatal outcomes in monoamniotic twins have been published (Table S3)[7,20–26]. In a retrospective study, Heyborne *et al.*[20] assessed the effectiveness of inpatient monitoring of monoamniotic twins, and observed improved neonatal survival among women who were admitted electively for inpatient monitoring. On the other hand, Van Mieghem *et al.*[22] concluded that if close fetal surveillance is instituted after 26–28 weeks and delivery takes place at approximately 32–34 weeks, the risk of perinatal complications is low, regardless of the surveillance setting.

Fetal demise is a major concern as a monoamniotic twin pregnancy approaches term, and early delivery would prevent this occurrence. It is indeed common for monoamniotic twins to be delivered preterm with planned Cesarean section at about 32 weeks' gestation[5,8]. In 2016, the Royal College of Obstetricians and Gynaecologists, ACOG and the Society for Maternal Fetal Medicine recommended that monoamniotic twin pregnancies should be delivered by Cesarean section between 32 and 33 weeks because of the high risk of intrauterine fetal death[8,27]. These recommendations are based on studies demonstrating that the perinatal mortality rate roughly doubles beyond 34 weeks (7%) compared with that at 33 weeks (4%)[4]. However, the justification for preterm delivery should be balanced against the likelihood of respiratory distress syndrome (5%) at 32 weeks[1,7], despite the use of antenatal steroids[28–30] in otherwise uncomplicated pregnancies[1,3,4,8]. This balance may not be achieved if fetal loss in uncomplicated monoamniotic twins is low[1,4]. Our study showed no fetal or neonatal death between 31 + 6 weeks and 36 + 6 weeks.

Conclusions

In uncomplicated monoamniotic twins, inpatient surveillance is associated with similar fetal mortality to that of outpatient management. As the raw rates of fetal mortality were 3.3% in the inpatient group and 10.8% in the outpatient group, further research is necessary.

Our data also suggest that, in non-anomalous uncomplicated monoamniotic twins, the fetal and neonatal death rates do not increase after 32 + 0 weeks, therefore planned Cesarean delivery at 33 + 0 to 34 + 6 weeks is a reasonable strategy to discuss with the patient. Data beyond 34 weeks are too limited to make a recommendation. Owing to the retrospective nature of this study, caution should be exercised before changes in practice are employed. A randomized controlled trial would provide the best evidence on the preferred method of monitoring for monoamniotic twins, however, this would be logistically difficult given the rarity of such pregnancies.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Table S1 Details of neonatal deaths according to gestational age at delivery

Table S2 Details of perinatal deaths according to gestational age at delivery

Table S3 Fetal death rates with inpatient and outpatient care, studies published since 2005

