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Original Research

Prediction of Monochorionic Diamniotic Twin Pregnancy Outcomes Based on Early Second Trimester Ultrasound

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Abstract

Background: Association between second trimester ultrasound findings and twin pregnancy outcome is still unclear. Study aimed to evaluate the performance of second trimester ultrasound scan in the prediction of monochorionic diamniotic twin pregnancies outcomes. **Methods**: Prospective-cohort study of all consecutive healthy women with monochorionic twin pregnancies followed-up and delivered in five years was undertaken. During second trimester screening (16–18 weeks) fetal biometry was measured (biparietal diameter–BPD, abdominal circumference–AC, femur length–FL, estimated fetal weight–EFW) and inter-twin discordance noted. Amniotic fluid amount was determined. Pregnancy outcomes were having live-born twins, Apgar sores and birth-weights, pregnancy complications and gestational week of delivery. **Results**: Receiver operating characteristics (ROC) analysis showed that BPD (p = 0.018), AC (p = 0.019) and FL (p = 0.015) were good predictors of having live-born twins. Regression analysis showed that the most important factors influencing twins' survival to term were inter-twin AC, BPD and FL differences. Fetal discordance in BPD, AC and FL explained correctly 76.3%, 76.5% and 58% of pregnancy outcomes. If second trimester inter-twin BPD difference was <2.5 mm, AC difference was <17 mm and FL difference was <1.5 mm survival of twins was better, complications were less frequent, delivery mostly occurred closer to term, twins had higher birth-weights and better Apgar scores. Second trimester EFW of twin and its difference as well as the amniotic fluid amount were not associated with examined pregnancy outcomes. **Conclusions**: Discordant twins' growth in the second trimester registered by ultrasound reliably implies on adverse monochorionic diamniotic twin pregnancy outcome.

Keywords: second trimester; ultrasound scan; monochorionic twins; pregnancy outcome; prediction models

1. Introduction

Monochorionic twin pregnancies are considered to have a high risk of perinatal morbidity and mortality, mainly from fetal growth restriction and preterm birth [1–3]. Other complications and causes of fetal death in these pregnancies include fetal anomalies, twin-twin transfusion syndrome (TTTS), tight cord entanglement, twin reversed arterial perfusion (TRAP), and acute hemodynamic imbalances due to large placental vascular anastomoses [4,5].

A priority in the management of monochorionic twin pregnancies is to identify patients at risk of adverse outcomes in order to offer appropriate and early intervention and to address any modifiable risk factors [1–3]. Current protocols suggest that monitoring monochorionic twins for potential complications should start from 16 weeks and should be repeated fortnightly until 24 weeks. At each ultrasound scan from 20 weeks, two or more biometric variables should be determined to estimate fetal weight discordance. Ultrasound scans should be performed at intervals of less than 28 days, and any difference in size between twins greater than 25% should be considered a clinically important indicator of intrauterine growth restriction. When discordant fetal growth is observed, patients should be referred to a tertiary-level fetal medical center [4,5].

Numerous studies have determined that inter-twin discordance detected in the early months of pregnancy is associated not only with later growth restriction but also with adverse outcomes. However, first-trimester crown-rump length (CRL) discordance seems to be of limited value in predicting poor pregnancy outcomes, as it is biased toward identifying twin pregnancy losses occurring before 20 gestational weeks (GW) [1–3,6].

On the other hand, the literature suggests that both disproportionate and proportionate fetal growth restriction may start in the second trimester, which may lead to poor perinatal outcomes [7]. Antenatal measurement of fetal abdominal circumference has proven to be the most sensitive ultrasound index for the detection of disturbances in fetal growth. Nevertheless, the association between second-trimester ultrasound biometry and adverse pregnancy outcomes in monochorionic twins has still not been thoroughly investigated [1,8].

Therefore, the aim of this study was to evaluate the performance of second-trimester ultrasound scans in the prediction of adverse perinatal outcomes in monochorionic diamniotic twin pregnancies.

2. Materials and Methods

A prospective cohort study was undertaken that included all consecutive monochorionic diamniotic twin pregnancies that were followed up and delivered during a five-year period (2010–2015) at the Clinic of Gynecology and Obstetrics Clinical Center of Serbia. There are currently no exact data on the prevalence of monochorionic diamniotic twins in Serbia, but in our clinic during the study period, their prevalence ranged from 0.1–0.4%. Twins' monochorionicity and diamnionicity was diagnosed by ultrasound usually during the first pregnancy check-up and at latest during the first trimester screening (Double test). After confirmation of the condition (a single placental mass with a negative lambda sign and an intra-amniotic membrane thinner than 2 mm), patients were closely monitored throughout their pregnancy. Gestational age was calculated according to Negel's rule and ultrasound biometric parameters. Medical history data, including the mothers' age and parity, the presence of comorbidities, and the mode of current pregnancy conception (spontaneous or by assisted reproduction technologies) were recorded for each patient. Exclusion criteria for the study included miscarriage before the eighth gestational week, genetic disorders in the twins, and chronic diseases in the mothers (e.g., diabetes, hypertension, heart disease, connective tissue diseases, hematological diseases, etc.) that might impact the course and outcome of the pregnancy. All patients provided their written consent to participate in the study, which was approved by the institution's Review Board (440/X-3).

At the 16th–18th GW, a second-trimester ultrasound was performed, during which, for both twins, biometric measurements (*i.e.*, biparietal diameter [BPD], abdominal circumference [AC], and femur length [FL]) were established. These measurements were used to determine the estimated fetal weight (EFW) of both twins. To evaluate the discordance between twins in the second trimester, we deducted the smaller/shorter value from the higher/longer value for each biometric parameter. In this way, the precise difference between the twins' biometric measures was obtained. Moreover, the deepest fluid pocket (DFP) was measured and used to assess the amount of amniotic fluid (oligohydramnios: DFP $<$2 cm; normal fluid amount: DFP 2–8 cm; polyhydramnios DFP $>$8 cm). In our study, the fluid amount was regarded as adequate if neither of the twins had any disturbances in the fluid amount.

Patients received regular follow-ups until delivery, and all pregnancy complications, such as intrauterine growth restriction, twin-to-twin transfusion syndrome, miscarriage (before the 24th GW), and premature delivery (24th–36th GW) were noted. Ultrasound monitoring of twins was performed using an ACCUVIX V10 device (Samsung Medison, Seoul, Republic of Korea), with a 3.75-MHz abdominal and s 45-Hz vaginal probe. Ultrasound examinations were performed for all women by the same sonographer (study author SA).

The primary positive pregnancy outcome that was assessed was the birth of live twins (one or both). Upon delivery, birth weight and Apgar sores were registered for all twins. The gestational week of delivery was also recorded and used as an additional measure of pregnancy outcome (term $\geq$36 GW).

Ultrasound data obtained for all twins in the second trimester were compared with the evaluated pregnancy outcomes. Data were analyzed using descriptive methods (percent, mean, standard deviation) and analytical statistics using IBM SPSS version 20 (IBM Corp., Armonk, NY, USA) for Windows. The correlations between ultrasound measurements and pregnancy outcomes were analyzed using Spearman's correlation coefficient. The significance of the differences between the parameters of twins was analyzed with the chi-squared, analysis of variance (ANOVA), and Kruskal–Wallis χ^2 (nonparametric ANOVA) tests.

Receiver operating characteristics (ROC) curve analysis was performed to set the cut-off values of the second-trimester ultrasound measures (the direct difference in BPD, AC, FL, and EFW between twins) that could impact pregnancy outcomes (live-born twins and delivery time) in our population. The parameters that explained a significant percentage of cases on ROC analysis were considered adequate predictors of having live-born twins. Inter-twin discordance in the second trimester was established if the difference in the biometric parameters between the larger and smaller twin was over the cut-off value determined by our ROC analysis. Finally, inter-twin differences in BPD, AC, FL, and EFW were categorized as under or over the cut-off value and were further assessed.

Univariate regression analysis was applied to evaluate and confirm the associations between monochorionic twin pregnancy outcomes (dependent variables: having live-born twins, week of gestation at delivery, birth weight, and the Apgar scores of twins) and the differences between the twins' second trimester ultrasound measures (the independent variables were the same for all regression analyses: AC, BPD, FL, EFW) along with the twins' amniotic fluid measurements.

3. Results

The study included 39 healthy women with monochorionic diamniotic twin pregnancies. The average age of the women was 30.85 $\pm$ 4.16 years of age. There were 21 (53.8%) male and 18 (46.2%) female twins. The examined women were mostly primiparous. Only three pregnancies were conceived by artificial reproductive technologies (ART). The mean values of the ultrasound parameters measured in the second trimester and the Apgar scores upon

Table 1. Parameters assessed in the second trimester and upon birth of monochorionic twin pregnancies.

Parameters (No 39)	Minimum	Maximum	Mean	Standard Deviation
Mothers age	24.00	40.00	30.85	4.16
Mothers parity	0.00	4.00	0.92	0.77
BPD twin 1 (mm)	24.00	52.00	35.08	6.19
BPD twin 2 (mm)	28.00	53.00	35.94	5.46
BPD direct difference	0.00	11.00	2.30	2.55
AC twin 1 (mm)	62.00	149.00	104.59	20.05
AC twin 2 (mm)	71.00	171.00	106.17	20.99
AC direct difference	0.00	65.00	11.45	15.75
FL twin 1 (mm)	13.00	32.00	19.99	4.26
FL twin 2 (mm)	16.00	32.00	20.35	3.74
FL direct difference	0.00	10.00	1.69	2.10
EFW twin 1 16–18 GW (gr)	100.00	192.00	136.46	23.83
EFW twin 2 16–18 GW (gr)	91.00	180.00	133.35	24.91
EFW direct difference	0.00	41.00	10.08	10.05
GW at birth (gr)	16.00	39.00	31.77	6.57
Twin 1 birth-weight (gr)	150.00	3100.00	1840.53	906.08
Twin 2 birth-weight (gr)	150.00	3100.00	1799.73	947.93
Twin 1 Apgar score	0.00	9.00	4.74	3.67
Twin 2 Apgar score	0.00	9.00	5.10	3.52

Legend: BPD, biparietal diameter; AC, abdominal circumference; FL, femur length; GW, gestational week; EFW, estimated fetal weight.

delivery of both twins are presented in Table 1. The gender of the twins did not correlate with pregnancy complications (p = 0.701) or outcomes (p = 0.217).

Generally, no significant differences were found between first and second twins regarding their mean ultrasound measures in the second trimester (BPD p = 0.516; AC p = 0.735; FL p = 0.698; EFW p = 0.461) or between the twins' birth weights (p = 0.849) or Apgar scores (p = 0.661) upon delivery.

The amount of amniotic fluid of the examined women was mostly adequate in the second trimester. There were a few cases of oligohydramnios and polyhydramnios, but polyhydramnios was more frequent than oligohydramnios in the second trimester.

Most twins were born live and without any complications (either diagnosed during pregnancy by ultrasound or upon birth). Out of 18 cases with complications, intrauterine growth restriction was registered in 14 (17.95%) fetuses, twin-to-twin transfusion syndrome in eight (20.51%) twin pairs, chorioamnionitis in six (15.38%), and preterm birth in eight (20.51%) pregnancies. No other complications, such as TRAP or vanishing twins, were noted.

Based on the ROC analysis, it was found that BPD, AC, and FL inter-twin differences between the 16th and 18th GW could be used as predictors of having live-born twins, while a second-trimester inter-twin difference in EFW was not proven to be a reliable indicator of pregnancy outcome. Moreover, raw measures of BPD, AC, and FL in both the first and second twin were also not significant. However, the EFW measure of both twins, assessed separately, was significantly associated with the twins' outcomes (Table 2).

Consequently, cut-off values for BPD, AC, and FL inter-twin differences for our population were established (2.5 mm, 17 mm, and 1.5 mm respectively). BPD, AC, and FL difference categories (under cut-off = adequate twin growth *vs.* over cut-off = discordant growth) accurately predicted the risk for adverse pregnancy outcomes in 76.3%, 76.5%, and 58.0% of the cases, respectively.

When these new biometry categories were further analyzed, it was seen that our sample contained significantly more twin pairs with a BPD difference of <2.5 mm and an AC difference of about 17 mm, while the number of twin pairs with FL differences of <1.5 mm and ≥1.5 mm was similar. Further descriptive information regarding the frequencies of the second-trimester ultrasound parameters and pregnancy outcome categories are shown in Table 3.

Having both twins born live significantly was negatively correlated with the amount of amniotic fluid and direct differences in the twins' BPD and AC, as well as with the BPD, AC, and FL difference categories (*i.e.*, under or over the cut-off value), while it was positively correlated with the FL and EFW of both twins. Better survival of monochorionic twins was achieved when the inter-twin difference in BPD was <2.5 mm, and the difference in AC was <17 mm, as well as when the FL of the twins was longer and the EFW higher in the second pregnancy trimester.

In cases where the difference in AC between the twins was about 17 mm, 29 twins were born live, but still there were cases of intra uterine fetal death. On the other hand,

Table 2. Coordinates and area under ROC (Receiver Operating Characteristics) curve which were used for determination of cut-off values of twins' second trimester biometry.

Parameters (No 39)	Area under ROC %	p	Cut-off values in mm/gr	Sensitivity %	Specificity %
BPD twin 1	59.6	0.386	33.5	56.7	44.4
BPD twin 2	59.6	0.386	33.5	70.0	44.4
BPD direct difference	76.3	0.018	2.5	66.7	80.0
FL twin 1	77.0	0.199	18.3	70.0	65.0
FL twin 2	64.3	0.474	18.5	70.0	66.7
FL direct difference	58.0	0.015	1.5	44.4	63.3
AC twin 1	56.7	0.549	95.0	73.0	44.4
AC twin 2	58.5	0.443	95.0	70.0	44.4
AC direct difference	76.5	0.019	17.0	55.6	96.7
EFW twin 1 grams	80.4	0.006	130.0	60.0	77.8
EFW twin 2 grams	84.8	0.002	120.5	73.3	77.8
EFW direct difference	45.4	0.677	5.5	53.3	44.4

Legend: BPD, biparietal diameter; AC, abdominal circumference; FL, femur length; EFW, estimated fetal weight.

Table 3. Further descriptive data regarding frequency of twins in different categories of evaluated second trimester ultrasound parameters and pregnancy outcomes.

Parameters (No 39)		Frequency	%	χ^2	p
Conception method	natural	36	92.3	27.923	0.001
	ART	3	7.7		
BPD difference new categories	<2.5 mm	27	69.2	5.769	0.016
	≥2.5 mm	12	30.8		
AC difference new categories	<17 mm	33	84.6	18.692	0.001
	≥17 mm	6	15.4		
FL difference new categories	<1.5 mm	24	61.5	2.077	0.150
	≥1.5 mm	15	38.5		
Amniotic fluid of twins	normal	30	76.9	35.231	0.001
	polyhydramnion	8	20.5		
	oligoamnion	1	2.6		
Delivery mode	vaginal	15	38.5	14.000	0.001
	Caesarean Section	24	61.5		
Complications	absent	21	53.8	0.641	0.423
	present	18	46.2		
Live-born twins	no–both twins	8	20.5	11.308	0.001
	no–one twin	1	2.6		
	yes–both live born	30	76.9		

Legend: BPD, biparietal diameter; AC, abdominal circumference; FL, femur length; ART, assisted reproduction techniques.

when the difference in AC between the twins in the second trimester was ≥17 mm, only one twin was born live. In cases where the difference in FL between the twins was about 1.5 mm, 19 twins were born live, and five twins did not survive even with adequate growth in the second trimester. Conversely, even with a difference in FL ≥1.5 mm, 10 twins were live-born.

The time of delivery was significantly negatively correlated with direct differences between the twins' BPD and AC, as well as the AC and FL difference categories (*i.e.*, under or over the cut-off) and was positively correlated with the twins' EFW. Delivery occurred in later gestational weeks when the second-trimester inter-twin difference in BPD was <2.5 mm, in AC was <17 mm, and in FL was <1.5 mm. Moreover, delivery was closer to term when the EWF of the twins in the second trimester was higher.

The Apgar scores of the twins were significantly negatively correlated with the amount of amniotic fluid, the direct difference between the twins' AC, and the AC difference categories (*i.e.*, above or below the cut-off) and were positively correlated with the EFW of the smaller twin. Monochorionic twins with a second-trimester inter-twin

AC difference <17 mm and higher EFW showed higher Apgar scores.

Twins' birth weights were significantly negatively correlated with the amount of amniotic fluid, the direct difference between the twins' AC, and the AC difference categories (*i.e.*, above or below the cut-off) and were positively correlated with the twins' EFW. The twins had higher birth weights when the AC difference between them in the second trimester was <17 mm and the EFW of both twins was higher.

Having complications during pregnancy correlated positively amniotic fluid, with AC difference categories, BPD and FL direct difference and difference in FL categories, and negatively with EFW of twins in the second trimester. The twins had fewer complications when the second-trimester inter-twin difference in BPD was about 2.5 mm, in AC was about 17 mm, and in FL was about 1.5 mm. Twins with a higher weight at 16–18 GW had fewer pregnancy complications.

Neither the mothers' age nor parity had a significant influence on any evaluated pregnancy outcome. Twins delivered by caesarean section had a better outcome. Table 4 shows the correlations between the second-trimester ultrasound twin measures and the evaluated pregnancy outcomes.

After finding numerous significant correlations between the examined parameters and pregnancy outcomes, univariate regression analysis was performed to assess the use of second-trimester ultrasound parameters to predict monochorionic diamniotic twin pregnancy outcomes. Tables 5,6 show the significant ultrasound parameters confirmed by the univariable regression analysis. No significant associations were found for twins' birth weight and Apgar sores.

Based on the obtained regression findings, it could be seen that direct difference in twins' AC as well as difference of twins' AC, BPD and FL according to newly set cutoffs were the most important predictors of having live-born twins. Moreover, direct differences in twins' AC and BPD as well as differences in twins' AC, BPD, and FL according to the newly set cut-offs were the most important predictors of gestational week of delivery. No other significant associations between second-trimester ultrasound parameters and pregnancy outcomes were confirmed by our regression analysis.

4. Discussion

Recently, attention has been drawn to the use of early-second-trimester ultrasound examinations to predict adverse perinatal outcomes [9]. Abnormal biometry has been confirmed in the literature as an independent contributor to the poor prognosis of twins. Moreover, it seems that ultrasound parameters have better predictive ability in monochorionic twins [10]. Based on the available literature, the current study is one of the few that have investigated the ability of second-trimester ultrasound parameters to predict outcomes in monochorionic diamniotic twin pregnancies.

It is well known that a suboptimal environment in early pregnancy may limit growth during the second and third trimesters [6,8]. It has been postulated that fetuses suffering from nutrient limitation during early pregnancy tend to be proportionately small at birth. Conversely, if growth restriction begins later in pregnancy due to pregnancy complications, fetuses are usually of normal length but lack adequate fat tissue deposits [11,12]. Some authors consider that fetuses that are smaller than expected at the mid-second-trimester ultrasound screening are likely already suffering from early growth restriction [3].

Discordant growth between twins can be one of the signs of pregnancy complications that begin in the first half of pregnancy [9,10]. A strong link between intrauterine growth restriction and TTTS or stillbirth has been found in numerous studies. These findings provide a rationale for using second-trimester fetal discordance to predict adverse outcomes [6,13]. Nevertheless, only a few previous studies have focused on the role of biometry discordance, assessed either by expected fetal weight or abdominal circumference measured at the time of the routine anomaly scan in the second trimester, in twin pregnancy outcomes [1,14]. Some studies indicate that a single biometric assessment of twins at 16 weeks detected 48% of later adverse outcomes. AC and EFW at 16 GW have been established as the most important predictors of adverse fetal outcomes as well as discordant twin growth [7,12,13].

One group of studies indicates that asymmetrically grown and discordant twins have worse perinatal outcomes (preterm birth and perinatal death) than symmetric twins [4,9]. Previous studies have reported that <25th percentile EFW discordance at the second-trimester ultrasound scan can be used to predict fetal loss [1,15,16]. Additionally, asymmetrically grown fetuses with a mean AC <2.5th percentile in the second trimester were more likely to have potentially lethal complications later in pregnancy. Inter-twin AC and EFW discordances are the only parameters that have been proven by numerous studies to reliably predict adverse obstetric outcomes [2,17]. Authors have reported that sensitivities for EFW or AC differences in discordant twins range from 33% to 93%, and specificities range from 68% to 99% [12,13].

Conversely, other studies have found that second-trimester ultrasound discordance in twins has poor predictive value for adverse perinatal outcomes, irrespective of chorionicity [1,18–20]. Although in some investigations, second-trimester EFW discordance correlated with birth-weight discordance ≥20–25%, the predictive accuracy was low, thus preventing its wide practical clinical use [7,8]. Once malformations, chromosomal abnormalities, and TTTS were excluded, second-trimester ultrasound discordance was not significantly correlated with subsequent adverse outcomes [1,7,8]. Moreover, in some studies, even

Table 4. Correlation of second trimester ultrasound parameters and pregnancy outcomes.

Parameters (No 39)		Live-born twins	GW	Apgar twin 1	Apgar twin 2	Twin 1 BW	Twin 2 BW	Complic
Age	ρ	0.210	0.111	0.075	0.171	0.162	0.117	–0.179
	p	0.200	0.500	0.649	0.298	0.330	0.490	0.275
Parity	ρ	0.001	0.059	0.000	–0.037	0.056	0.027	0.326
	p	0.995	0.723	1.000	0.825	0.737	0.875	0.672
Conception method	ρ	0.249	0.158	0.178	0.195	0.134	0.204	–0.267
	p	0.126	0.336	0.278	0.235	0.424	0.226	0.100
Delivery mode	ρ	0.693	0.485	0.395	0.417	0.346	0.361	–0.431
	p	0.001	0.002	0.013	0.008	0.033	0.028	0.006
AC twin 1	ρ	–0.062	0.097	–0.051	–0.110	–0.144	–0.227	0.098
	p	0.708	0.555	0.758	0.506	0.389	0.176	0.551
AC twin 2	ρ	0.035	0.124	0.042	0.003	–0.091	0.005	–0.053
	p	0.831	0.450	0.801	0.983	0.586	0.975	0.751
AC direct difference	ρ	–0.468	–0.389	–0.518	–0.372	–0.349	–0.371	0.241
	p	0.003	0.014	0.002	0.020	0.032	0.025	0.139
AC new categories	ρ	–0.534	–0.610	–0.507	–0.540	–0.466	–0.453	0.461
	p	0.001	0.001	0.001	0.001	0.003	0.005	0.003
BPD twin 1	ρ	–0.030	0.141	–0.047	–0.101	–0.095	–0.130	0.009
	p	0.856	0.391	0.776	0.542	0.571	0.442	0.956
BPD twin 2	ρ	0.014	0.141	0.023	–0.038	–0.048	0.089	0.039
	p	0.934	0.391	0.890	0.820	0.773	0.601	0.814
BPD direct difference	ρ	–0.395	–0.361	–0.230	–0.239	–0.382	–0.321	0.360
	p	0.013	0.024	0.159	0.142	0.018	0.052	0.025
BPD new categories	ρ	–0.426	–0.191	–0.241	–0.195	–0.289	–0.163	0.386
	p	0.007	0.244	0.140	0.234	0.079	0.336	0.015
FL twin 1	ρ	0.126	0.397	0.142	0.064	0.046	–0.010	–0.140
	p	0.445	0.012	0.387	0.697	0.782	0.951	0.395
FL twin 2	ρ	0.059	0.399	0.064	–0.023	–0.116	0.027	–0.120
	p	0.720	0.011	0.699	0.891	0.490	0.874	0.469
FL direct difference	ρ	–0.327	–0.120	–0.152	–0.185	–0.267	–0.226	0.339
	p	0.042	0.466	0.356	0.260	0.105	0.178	0.035
FL new categories	ρ	–0.226	–0,267	–0.093	–0.114	–0.179	–0.135	0.520
	p	0.166	0.044	0.574	0.490	0.281	0.425	0.007
EFW twin 1	ρ	0.444	0.503	0.268	0.298	0.482	0.405	–0.482
	p	0.005	0.001	0.098	0.066	0.002	0.013	0.002
EFW twin 2	ρ	0.509	0.491	0.318	0.323	0.417	0.337	–0.487
	p	0.001	0.002	0.048	0.045	0.009	0.041	0.002
EFW direct difference	ρ	–0.068	–0.053	–0.073	–0.150	–0.081	–0.173	0.190
	p	0.682	0.748	0.659	0.362	0.630	0.306	0.246
Amniotic fluid of twins	ρ	–0.536	–0.262	–0.391	–0.486	–0.540	–0.589	0.471
	p	0.000	0.107	0.014	0.002	0.000	0.000	0.002

Legend: Complic, complications; AC, abdominal circumference; BPD, biparietal diameter; FL, femur length; EFW, estimated fetal weight; GW, gestational week; BW, birth weight.

after adjusting for monochorionicity, the predictive value of using either second-trimester EFW or AC discordance did not improve [1,19]. These findings may be explained by the fact that discordant growth and other complications may appear only late in gestation [10]. In some investigations, growth restriction in fetuses was not detected in the second trimester. However, increased ultrasound surveillance is advisable whenever small or discordant twins are diagnosed in early pregnancy [2,18,20].

The findings of our study are in accordance with the findings of previous studies that the biometric parameters of twins at 16 to 18 GW could be used as predictors of hav-

Table 5. Regression analysis of second trimester ultrasound parameters impact on having live-born twins.

Parameters	Coefficient B	Coefficient Wald	p	Odds ratio	95% confidence interval for odds ratio	
					Lower bound	Upper bound
AC direct difference	–0.073	5.812	0.016	0.930	0.876	0.986
AC new categories	–3.590	8.684	0.003	0.028	0.003	0.300
BPD new categories	–2.079	6.105	0.013	0.125	0.024	0.651
FL new categories	–0.362	4.725	0.030	0.696	0.502	0.965

Legend: AC, abdominal circumference; BPD, biparietal diameter; FL, femur length.

Table 6. Regression analysis of the second trimester ultrasound parameters influence on the time of delivery.

Parameters	Unstandardized coefficients		Standardized coefficients	p	95% confidence interval for B	
	B	Standard error	Beta		Lower bound	Upper bound
AC direct difference	–0.242	0.056	–0.579	0.001	–0.355	–0.128
AC new categories	–11.152	2.318	–0.620	0.001	–15.849	–6.454
BPD direct difference	–1.209	0.374	–0.470	0.003	–1.967	–0.452
BPD new categories	–4.722	2.176	–0.336	0.037	–9.132	–0.313
FL new categories	–0.994	0.487	–0.318	0.049	–1.982	–0.006

Legend: AC, abdominal circumference; BPD, biparietal diameter; FL, femur length.

ing live-born twins [1,6,11]. Inter-twin differences in BPD, AC, and FL detected early in the second trimester reliably predict pregnancy outcomes.

The cut-off for AC inter-twin difference in our sample corresponds with value suggested in the literature (17 mm) [2,13]. However, ours is the first study to establish a cut-off value for BPD and FL inter-twin differences. In our study, fetal discordance correctly predicted the risk of adverse pregnancy outcomes in more than 50% of the twins. Nevertheless, it should be noted that the sensitivity of all these measurements was not high. On the other hand, discordance in AC and BPD was ≥80%.

According to our regression analysis, the most important predictors of having two live-born monochorionic twins were inter-twin AC, BPD, and FL differences categorized according to our newly proposed cut-off values. Our findings indicate that when the second-trimester inter-twin AC difference was about 17 mm, BPD was about 2.5 mm, and the difference in FL was about 1.5 mm, the survival of both twins was more likely, and delivery was more likely to occur closer to term. Thus, the discordant growth of twins in the second trimester was confirmed to correlate with adverse pregnancy outcomes.

The major limitation of our study is the small sample size, which impacts the generalizability and statistical relevance of the results. Moreover, our conclusions could be biased because the study did not include a control group. However, monochorionic twin pregnancies are quite rare compared to other pregnancy types. Therefore, the post-hock power of the study was good (71.2%). We plan to conduct further studies with larger samples in clinical practice to construct multivariable models for predicting the outcomes of monochorionic diamniotic twin pregnancy. Due to the rarity of of monochorionic diamniotic twins and consequently information regarding them our data would be useful for being assessed in an individual patient meta-analysis.

5. Conclusions

Discordant growth of twins along with amniotic fluid disturbances registered on the second trimester ultrasound scan can be used as reliable sign of potential adverse outcomes of monochorionic diamniotic twins. According to regression analysis performed in our study inter-twin AC, BPD and FL differences are biometric parameters of most importance when assessing monochorionic diamniotic twins. If second trimester amniotic fluid is adequate, inter-twin BPD difference is <2.5 mm, AC difference is <17 mm and difference in FL is <1.5 mm survival of twins is better, complications are less frequent, delivery mostly occurs closer to term, twins have higher birth-weight and better Apgar scores.

Availability of Data and Materials

The data presented in this study are available on request from the corresponding author, but not publicly available as we present personal patients' findings.

Author Contributions

SA, DKB and IB designed the research study. SA, JD and DKB analyzed the data. MMC, IV, MM and SM performed the research, interpreted the findings and performed the literature review. SA, DKB, JD, IV wrote the manuscript. SP and SB critically revised the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

All investigated women signed informed consent for the study. The study was approved by the Review Board of Medical Faculty University of Belgrade (440/X-3).

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Conflict of Interest

The authors declare no conflict of interest.

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