First trimester ultrasonographic parameters in prediction of the course and outcome of monochorionic twin pregnancies

Slavica AKSAM1,*, Snezana PLESINAC1,2, Jelena DOTLIC1, Jasmina TADIĆ, Svetlana VRZIC-PETRONIJEVIC1,2, Milos PETRONIJEVIC1,2, Dusica KOCIJANCIC-BELOVIC1, Snezana BUZADZIC1
1Clinic of Obstetrics and Gynecology, Clinical Center of Serbia, Belgrade, Serbia
2Faculty of Medicine, University of Belgrade, Belgrade, Serbia

1. Introduction
Monochorionic twin pregnancies carry a high perinatal risk and have the most adverse pregnancy outcomes. Apart from the usual complications occurring in singleton or dichorionic twin pregnancies, unique type-specific perinatal complications, such as twin-to-twin transfusion syndrome, develop more often in these pregnancies (1–3). Therefore, increased detailed antenatal fetal surveillance with precise first-trimester diagnosis of chorionicity is suggested for those twins (4,5).

The growth discordance of monochorionic diamniotic twins has been associated with adverse pregnancy outcomes and fetal loss. Recent evidence suggests that divergent growth patterns may begin as early as the first trimester (6,7). Ultrasonographic measurements of twins’ biometry, crown-rump length (CRL), nuchal translucency (NT), and amniotic fluid are the most commonly applied methods for pregnancy surveillance and diagnosing perinatal complications. These ultrasonographic measurements are used to assess early first-trimester intertwin discrepancy. Although there have been numerous efforts to associate with adverse perinatal outcomes, studies have reported inconsistent findings (8,9).

The aim of this study was to evaluate the association and the potential predictive value of first trimester ultrasonographic parameters on the course and outcome of monochorionic diamniotic twin pregnancies.

2. Materials and methods
2.1. Subjects and methods
A prospective cohort study was undertaken of 39 healthy women with consecutive monochorionic diamniotic twin pregnancies. During first-trimester screening, crown-rump length (CRL) and nuchal translucency (NT) were measured. The intertwin discordance in CRL and NT was determined. As pregnancy outcomes we assessed twins’ live-born rates, Apgar scores, birth weight, pregnancy complications, and gestational week of delivery.

Results: None of the assessed pregnancy outcomes significantly correlated with standard CRL discordance ≥10%. The newly established cut-off was 3.75 mm for CRL and 1.3 mm for NT. Monochorionic diamniotic twins were delivered in a later gestational week and had better chance of survival if CRL intertwin difference was <3.75 mm. Apgar scores significantly negatively correlated only with NT of corresponding twins. When intertwin NT difference was ≥1.3 mm, twins had lower birth weight and pregnancy complications were more frequent. Regression models show that intertwin CRL difference <3.75 mm is a significant predictor of live-born monochorionic diamniotic twins.

Conclusion: CRL and NT in monochorionic diamniotic twin pregnancies could indicate pregnancy complications and outcomes.

Keywords: Crown-rump length, first trimester ultrasound, monochorionic diamniotic twins, nuchal translucency, pregnancy outcomes

* Correspondence: slavicakasam@gmail.com

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and Obstetrics of the Clinical Center of Serbia. After ultrasonographic confirmation of twin monochorionicity and diaminicnity (single placental mass with negative lambda sign and intraamniotic membrane thinner than 2 mm), women were closely monitored throughout pregnancy. Medical history such as age, parity, presence of comorbidities, and mode of current pregnancy conception (spontaneous or using assisted reproduction techniques (ART)) was determined for all the women. Exclusion criteria for this study were miscarriage before the eighth gestational week, genetic disorders of twins, and existence of chronic diseases in mothers (diabetes, hypertension, heart disease, connective tissue diseases, hematological diseases, etc.) that could influence the pregnancy course and outcome. The study was approved by the institutional review board. All patients signed a written informed consent form.

Monitoring of twins was performed by ultrasound biometry examinations with an ACCUVIX device (Samsung Medison, Seoul, South Korea), with 3.75-MHz abdominal and vaginal probes. At the 12th/13th week of gestation, a mandatory first trimester screening (double test) was performed for both twins, i.e. CRL and NT were measured to the nearest millimeter in the sagittal section of the fetus, with the head in a neutral position. The intertwin discordance in CRL and NT was calculated by deducting the smaller/shorter from the higher/longer value. Achieved difference was then expressed as a percentage of the larger measurement. When the CRL difference was over 10% of the longer twin length, it was considered discordant. The amount of amniotic fluid was measured and categorized as oligoamnion, of normal amount, and polyhydramnion, based on the deepest fluid pocket (DFP): oligoamenomnia < 2 cm; normal fluid 2–8 cm; polyhydramnion > 8 cm.

Throughout the second and third pregnancy trimesters, patients were regularly checked. We noted all pregnancy complications such as intrauterine growth restriction, twin-to-twin transfusion syndrome, miscarriage, and premature delivery (before the 24th gestational week).

The main positive pregnancy outcome assessed in this study was having live-born twins (one or both). Apgar scores upon delivery and gestational week of delivery were registered for all twins. We also recorded whether the membranes ruptured prematurely preterm (PPROM) or during delivery. The quality of amniotic fluid on delivery was categorized as clear/milky, which was considered a good finding, or cloudy/green/bloody, which was regarded as an adverse finding. After delivery, all placentas were histopathologically (HP) examined and the presence of chorioamnionitis or vascular pathologies was recorded.

2.2. Statistical analysis

Ultrasonographic data obtained for all twins in the first trimester were compared with evaluated pregnancy outcomes. Data were analyzed with methods of descriptive (percent, mean, standard deviation (SD), median, interquartile range (IR)) and analytical statistics, using SPSS 20 (IBM SPSS version 22.0, Chicago, IL, USA). Correlations of ultrasonographic measurements and pregnancy outcomes were tested using Spearman correlation (ρ). Significance of differences between categories of assessed parameters was examined by χ² test and Kruskal–Wallis nonparametric ANOVA (KW χ²).

The ability of CRL and NT to discriminate between adverse and favorable pregnancy outcomes was described by receiver operator characteristic curve statistics (ROC), using varying cut-off levels of CRL and NT.

Finally, we applied enter and forward Wald binary logistic regression and enter and step-wise multiple linear regression to construct models of monochorionic twin pregnancy outcomes prediction, based on first trimester ultrasonographic parameters. All models were adjusted for potential confounders (mothers’ age, parity, and method of conception).

3. Results

The study included 39 healthy women with monochorionic diamniotic twin pregnancies of average 30.8 ± 4.2 years of age. The examined women were mostly primiparous (P = 0.001). Only three pregnancies were conceived by ART (P = 0.001). The average values of ultrasonographic parameters measured in the first trimester and the mean Apgar scores upon delivery of both twins are presented in Table 1. Mothers’ age and values of twins’ CRL and NT were P > 0.05, whereas other descriptive parameters were not normally distributed. Frequencies of first trimester ultrasonographic parameters and pregnancy outcomes categories are shown in Table 2.

There were no significant differences between the first and second twin regarding their ultrasonographic measures in the first pregnancy trimester (CRL P = 0.601; NT P = 0.428) or between twins’ Apgar scores upon delivery (Apgar score P = 0.661).

There were no cases of oligoamnion and very few of polyhydramnion in the first trimester. There was a similar number of twin pairs with CRL difference <10% and ≥10% of their length (Table 2). Most twins were live-born and did not have any complications (either ultrasonographically diagnosed during pregnancy or upon birth). Out of 18 cases of complications, intrauterine growth restriction (IUGR) was registered in 14 (17.95%) fetuses, twin-to-twin transfusion syndrome (TTTS) in 8 (20.51%) twin pairs, chorioamnionitis in 6 (15.38%) pregnancies, and preterm birth in 8 (20.51%) pregnancies. No other complications were noted. Histopathological examination of placentas revealed that there were no significant differences in
frequency of normal findings and vascular pathologies (Table 2).

Since having both twins live-born was not significantly correlated with CRL discordance ≥10%, we performed receiver operating characteristics (ROC) analysis to determine the cut-off values of CRL intertwin difference for our population. Based on the significant percent of explained cases through ROC analysis, we found that NT could also be a predictor of having twins live-born, whereas first-trimester DFP measurements were not proven as a significant predictor. Consequently, cut-off values of NT for our population were established. CRL and NT were recategorized (under or over the new cut-off) and assessed in such manner. The new cut-off for CRL had better specificity, whereas the sensitivity of new NT cut-off value was quite high (Table 3).

Tables 4 and 5 present correlations of ultrasonographic first-trimester twin measures with the evaluated pregnancy outcomes.

Having both monochorionic twins live-born was significantly negatively correlated with CRL discordance between twins, based on our new cut-off levels. Better survival of monochorionic diamniotic twins was achieved when CRL difference between twins was <3.75 mm (KW \( \chi^2 = 4.690; P = 0.030 \)). No other ultrasonographic parameters measured in the first trimester had significant influence on having twins live-born (P > 0.05).

Out of all assessed first trimester ultrasonographic parameters, twins’ Apgar scores significantly negatively correlated only with the NT of the corresponding twin. When NT in the first trimester was longer than the referral, twins had lower Apgar scores upon delivery. Still, there were no significant differences between twins’ Apgar scores regarding any discordance between twins in the first pregnancy trimester (P > 0.05).

Birth weight of both twins correlated negatively with newly established categories of NT, based on our cut-off levels. When NT difference between twins was >1.3 mm, twins had lower birth weight. However, there were no significant differences between twins’ birth weight regarding any of the ultrasonographic parameters of twins in the first pregnancy trimester (P > 0.05).

The time of delivery, i.e. gestational week (GW), was negatively correlated only with new CRL categories for our patients. Preterm delivery of monochorionic diamniotic twins occurred more often when CRL difference between twins was >3.75 mm (KW \( \chi^2 = 4.330; P = 0.001 \)).

Fetal complications were significantly positively correlated with the NT of both twins, i.e. NT direct difference and newly established categories of NT based on our cut-off levels. Fetal complications in monochorionic diamniotic twins occurred less often when NT of both twins was <95% (2 mm) and when the difference between twins’ NT measurements was <1.3 mm. Moreover, significant differences were registered in the occurrence of complications if NT values of first (KW \( \chi^2 = 6.498; P = 0.039 \)) and second (KW \( \chi^2 = 7.683; P = 0.031 \)) twin were above the referral values. Nevertheless, no other first trimester ultrasonographic parameters had significant influence on the presence of fetal complications in monochorionic diamniotic twin pregnancies (P > 0.05).

### Table 1. Parameters assessed in the first trimester and upon birth of monochorionic diamniotic twin pregnancies.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>IR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother’s age</td>
<td>24.0</td>
<td>40.0</td>
<td>30.8</td>
<td>4.2</td>
<td>30.00</td>
<td>5.00</td>
</tr>
<tr>
<td>Mother’s parity</td>
<td>0.00</td>
<td>4.00</td>
<td>0.92</td>
<td>0.77</td>
<td>0.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Twin 1 CRL (mm)</td>
<td>45.00</td>
<td>72.60</td>
<td>55.95</td>
<td>7.58</td>
<td>55.00</td>
<td>9.70</td>
</tr>
<tr>
<td>Twin 1 NT (mm)</td>
<td>0.90</td>
<td>2.80</td>
<td>1.54</td>
<td>0.33</td>
<td>1.60</td>
<td>0.32</td>
</tr>
<tr>
<td>Twin 2 CRL (mm)</td>
<td>45.00</td>
<td>70.30</td>
<td>54.98</td>
<td>8.64</td>
<td>54.90</td>
<td>8.00</td>
</tr>
<tr>
<td>Twin 2 NT (mm)</td>
<td>1.00</td>
<td>3.30</td>
<td>1.60</td>
<td>0.40</td>
<td>1.60</td>
<td>0.50</td>
</tr>
<tr>
<td>NT direct difference (mm)</td>
<td>0.00</td>
<td>0.60</td>
<td>0.22</td>
<td>0.18</td>
<td>0.19</td>
<td>0.23</td>
</tr>
<tr>
<td>CRL direct difference (mm)</td>
<td>0.00</td>
<td>20.00</td>
<td>3.61</td>
<td>3.68</td>
<td>3.68</td>
<td>3.90</td>
</tr>
<tr>
<td>GW birth/miscarriage</td>
<td>16.00</td>
<td>39.00</td>
<td>31.77</td>
<td>6.57</td>
<td>34.00</td>
<td>7.00</td>
</tr>
<tr>
<td>Twin 1 birth weight (g)</td>
<td>150.00</td>
<td>3100.00</td>
<td>1840.53</td>
<td>906.08</td>
<td>2100.00</td>
<td>1290.00</td>
</tr>
<tr>
<td>Twin 1 Apgar score</td>
<td>0.00</td>
<td>9.00</td>
<td>4.74</td>
<td>3.67</td>
<td>7.00</td>
<td>7.00</td>
</tr>
<tr>
<td>Twin 2 birth weight (g)</td>
<td>150.00</td>
<td>3100.00</td>
<td>1799.73</td>
<td>947.93</td>
<td>2000.00</td>
<td>1885.00</td>
</tr>
<tr>
<td>Twin 2 Apgar score</td>
<td>0.00</td>
<td>9.00</td>
<td>5.10</td>
<td>3.52</td>
<td>6.00</td>
<td>7.00</td>
</tr>
</tbody>
</table>

CRL: crown rump length; GW: gestational week; NT: nuchal translucence; SD: standard deviation; IR: interquartile range.

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Table 2. Frequency of twins regarding different categories of evaluated first trimester ultrasonographic parameters and pregnancy outcomes.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Frequency</th>
<th>%</th>
<th>$\chi^2$</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conception method</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Natural</td>
<td>36</td>
<td>92.3</td>
<td>27.923</td>
<td>0.001</td>
</tr>
<tr>
<td>ART</td>
<td>3</td>
<td>7.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRL 10% standard categories</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10%</td>
<td>31</td>
<td>39.7</td>
<td>13.564</td>
<td>0.001</td>
</tr>
<tr>
<td>≥10%</td>
<td>8</td>
<td>10.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRL our new cut-off</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3.75 mm</td>
<td>25</td>
<td>64.1</td>
<td>3.103</td>
<td>0.078</td>
</tr>
<tr>
<td>≥3.75 mm</td>
<td>14</td>
<td>35.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NT our new cut-off</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1.3 mm</td>
<td>18</td>
<td>46.2</td>
<td>0.231</td>
<td>0.631</td>
</tr>
<tr>
<td>≥1.3 mm</td>
<td>21</td>
<td>53.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Twin 1 DFP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>37</td>
<td>94.9</td>
<td>31.410</td>
<td>0.001</td>
</tr>
<tr>
<td>Polyhydramnion</td>
<td>2</td>
<td>5.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Twin 2 DFP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>37</td>
<td>94.9</td>
<td>31.410</td>
<td>0.001</td>
</tr>
<tr>
<td>Polyhydramnion</td>
<td>2</td>
<td>5.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delivery type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal</td>
<td>15</td>
<td>38.5</td>
<td>14.000</td>
<td>0.001</td>
</tr>
<tr>
<td>Caesarean section</td>
<td>24</td>
<td>61.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Live-born twins</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No – both twins</td>
<td>8</td>
<td>20.5</td>
<td>11.308</td>
<td>0.001</td>
</tr>
<tr>
<td>No – one twin</td>
<td>1</td>
<td>2.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes – both live-born</td>
<td>30</td>
<td>76.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>21</td>
<td>53.8</td>
<td>0.641</td>
<td>0.423</td>
</tr>
<tr>
<td>Present</td>
<td>18</td>
<td>46.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amniotic rupture</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On term</td>
<td>32</td>
<td>82.1</td>
<td>16.026</td>
<td>0.001</td>
</tr>
<tr>
<td>PPROM</td>
<td>7</td>
<td>17.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amniotic fluid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clear/milky</td>
<td>29</td>
<td>74.4</td>
<td>9.256</td>
<td>0.002</td>
</tr>
<tr>
<td>Cloudy/green/bloody</td>
<td>10</td>
<td>25.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placental histopathology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without pathology</td>
<td>15</td>
<td>38.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular pathologies</td>
<td>18</td>
<td>46.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>6</td>
<td>15.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ART: assisted reproduction; CRL: crown rump length; DFP: deepest fluid pocket; NT: nuchal translucence; PPROM: premature preterm amniotic rupture.

Table 3. Coordinates and the area under ROC curve that were used for the determination of the cut-off values of the investigated parameters in our sample.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Area under ROC %</th>
<th>Cut-off values in mm</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Twin 1 CRL</td>
<td>46.3</td>
<td>53.5</td>
<td>63.3</td>
<td>44.4</td>
</tr>
<tr>
<td>Twin 2 CRL</td>
<td>51.7</td>
<td>53.5</td>
<td>63.3</td>
<td>44.4</td>
</tr>
<tr>
<td>CRL our new cut-off</td>
<td>64.8</td>
<td>3.75</td>
<td>66.7</td>
<td>73.3</td>
</tr>
<tr>
<td>Twin 1 NT</td>
<td>66.9</td>
<td>1.55</td>
<td>77.8</td>
<td>55.3</td>
</tr>
<tr>
<td>Twin 2 NT</td>
<td>69.6</td>
<td>1.55</td>
<td>66.7</td>
<td>50.0</td>
</tr>
<tr>
<td>NT our new cut-off</td>
<td>60.6</td>
<td>1.3</td>
<td>77.8</td>
<td>53.3</td>
</tr>
</tbody>
</table>

CRL: crown rump length; NT: nuchal translucence.
Out of all examined first trimester parameters, the quality of amniotic fluid significantly negatively correlated only with the method of conception. In addition, if twins’ NT measures were over the cut-off levels, the amniotic fluid was significantly more often cloudy/green/bloody (twin 1 KW $\chi^2 = 4.365; P = 0.037$, and twin 2 KW $\chi^2 = 5.567; P = 0.018$).

Table 4. Correlations of ultrasonographic first trimester parameters with pregnancy outcomes.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Live-born twins</th>
<th>Apgar twin 1</th>
<th>Apgar twin 2</th>
<th>GW</th>
<th>Twin 1 birth weight</th>
<th>Twin 2 birth weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>$\rho$</td>
<td>0.111</td>
<td>0.075</td>
<td>0.171</td>
<td>0.210</td>
<td>0.162</td>
</tr>
<tr>
<td></td>
<td>$P$</td>
<td>0.500</td>
<td>0.649</td>
<td>0.298</td>
<td>0.200</td>
<td>0.330</td>
</tr>
<tr>
<td>Parity</td>
<td>$\rho$</td>
<td>0.059</td>
<td>0.000</td>
<td>-0.037</td>
<td>0.001</td>
<td>0.056</td>
</tr>
<tr>
<td></td>
<td>$P$</td>
<td>0.723</td>
<td>1.000</td>
<td>0.825</td>
<td>0.995</td>
<td>0.737</td>
</tr>
<tr>
<td>Conception method</td>
<td>$\rho$</td>
<td>0.158</td>
<td>0.178</td>
<td>0.195</td>
<td>0.249</td>
<td>0.134</td>
</tr>
<tr>
<td></td>
<td>$P$</td>
<td>0.336</td>
<td>0.278</td>
<td>0.235</td>
<td>0.126</td>
<td>0.424</td>
</tr>
<tr>
<td>Twin 1 CRL</td>
<td>$\rho$</td>
<td>-0.054</td>
<td>0.061</td>
<td>-0.026</td>
<td>0.085</td>
<td>0.045</td>
</tr>
<tr>
<td></td>
<td>$P$</td>
<td>0.743</td>
<td>0.713</td>
<td>0.875</td>
<td>0.609</td>
<td>0.790</td>
</tr>
<tr>
<td>Twin 1 DFP</td>
<td>$\rho$</td>
<td>0.127</td>
<td>0.121</td>
<td>0.152</td>
<td>0.182</td>
<td>0.102</td>
</tr>
<tr>
<td></td>
<td>$P$</td>
<td>0.440</td>
<td>0.464</td>
<td>0.357</td>
<td>0.268</td>
<td>0.541</td>
</tr>
<tr>
<td>Twin 1 NT</td>
<td>$\rho$</td>
<td>-0.248</td>
<td>-0.357</td>
<td>-0.284</td>
<td>-0.271</td>
<td>-0.173</td>
</tr>
<tr>
<td></td>
<td>$P$</td>
<td>0.128</td>
<td>0.025</td>
<td>0.079</td>
<td>0.095</td>
<td>0.299</td>
</tr>
<tr>
<td>Twin 2 CRL</td>
<td>$\rho$</td>
<td>0.024</td>
<td>0.049</td>
<td>-0.073</td>
<td>0.087</td>
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<td>$\rho$</td>
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<td>$\rho$</td>
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<td>$P$</td>
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<tr>
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<td>$P$</td>
<td>0.028</td>
<td>0.123</td>
<td>0.083</td>
<td>0.024</td>
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</table>

Apgar: Apgar score; CRL: crown rump length; DFP: deepest fluid pocket; GW: gestational week of birth/miscarriage; NT: nuchal translucence.

Out of all examined first trimester parameters, the quality of amniotic fluid significantly negatively correlated only with the method of conception. In addition, if twins’ NT measures were over the cut-off levels, the amniotic fluid was significantly more often cloudy/green/bloody (twin 1 KW $\chi^2 = 4.365; P = 0.037$, and twin 2 KW $\chi^2 = 5.567; P = 0.018$).

Time of amniotic rupture and histopathological findings of placenta were positively correlated with NT measures of both twins. However, there were no significant differences in placental HP findings regarding any discordance between twins in the first pregnancy trimester ($P > 0.05$). Still, when twins’ NT in the first trimester was longer than the referral by 95% (2 mm), the PPROM was more frequent (twin 1 KW $\chi^2 = 3.888; P = 0.049$, and twin 2 KW $\chi^2 = 3.888; P = 0.049$). Neither mothers’ age nor parity had significant influence on any evaluated pregnancy outcome. All twins conceived by ART in our sample had appropriate quality of amniotic fluid. The amount of amniotic fluid in the first trimester did not show a significant relationship with any of the assessed pregnancy outcomes.
After confirmation of significant correlations between the examined parameters, we constructed models of monochorionic diamniotic twin pregnancy outcomes prediction, based on first trimester ultrasonographic parameters. There were no confounders in our analysis.

When enter and forward Wald binary logistic regression was applied to assess the influence of all ultrasonographic parameters on having twins live-born, a significant equation was obtained ($\chi^2 = 4.668; P = 0.031$; $B = 1.240$; Wald = 10.035; Exp(B) = 3.333; $R^2$ Nagelkerke = 0.171; total classification = 76.9%):

\[
\text{LIVE-BORN TWINS} = 1.992 - 1.705 \times \text{CRL NEW CUTOFF} (< / \geq 3.75 \text{ mm})
\]

Enter and step-wise multiple linear regression was used to investigate the influence of all first trimester ultrasonographic measures on the time of delivery (gestational week of birth/miscarriage), and a significant equation was achieved ($R = 0.592; \text{adj}R^2 = 0.229; F = 2.880; P = 0.023$):

\[
\text{DELIVERY TIME} = 39.502 - 0.923 \times \text{CRL DIRECT DIFFERENCE}
\]

4. Discussion
The results presented in this study show that the most important predictor of better survival of monochorionic diamniotic twins is the intertwin CRL difference, which is $<3.75$ mm. No other first trimester ultrasonographic

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Delivery type</th>
<th>Complications yes/no</th>
<th>Amnion rupture</th>
<th>Amniotic fluid</th>
<th>Placenta HP</th>
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<td>Age</td>
<td>$\rho$ 0.205</td>
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<td>$-0.221$</td>
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<td>0.383</td>
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<td>$-0.109$</td>
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<tr>
<td>$P$ 0.277</td>
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<td>0.510</td>
<td>0.096</td>
<td>0.407</td>
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<td>$-0.109$</td>
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<td>$-0.137$</td>
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<td>$P$ 0.277</td>
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<td>0.510</td>
<td>0.096</td>
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<td>0.773</td>
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CRL: crown rump length; DFP: deepest fluid pocket; HP: histopathology; NT: nuchal translucence.
parameters had significant influence on having twins live-born. Direct difference in twins’ CRL can be used to reliably predict the gestational week in which the delivery might occur. When NT difference between twins is >1.3 mm, twins have lower birth weight, and pregnancy complications develop more often. Moreover, twins have lower Apgar scores upon delivery when first trimester NT is longer than the referral by 95% (2 mm).

The number and frequency of multiple pregnancies is constantly growing, mainly due to assisted reproduction with ovulation stimulation, and now accounts for about 3% of all pregnancies (6). The role of ultrasound in the control of these pregnancies is essential, because it enables the diagnosis of specific entities for multiple pregnancy such as type of chorionicity and placentation, discordant growth, and twin-to-twin transfusion syndrome (5,7).

The assessment of chorionicity is of great importance in pregnancy surveillance and in the prediction of possible perinatal disorders (2). The importance of determining chorionicity lies in the fact that it is directly linked to complications in pregnancy (1). Miscarriage rates between the 12th and 24th week of gestation are six times higher in monochorionic twins. In addition, single or double fetal loss after the 24th gestational week was proven to be significantly higher in monochorionic (17.53%) than in dichorionic (3.95%) twins (10).

Various studies reported that twins’ size discordance in the first trimester of pregnancy increases the risk of pregnancy complications, including miscarriages and/or preterm births, twin-to-twin transfusion syndrome, late pregnancy growth discrepancy, congenital malformations, and fetal death (8,11,12). Early detection of a subgroup of these high-risk complications would be useful in the management of twin pregnancies (7).

Studies showed that monochorionic diamniotic twin pregnancies with subsequent pregnancy loss presented increased discrepancy between twins in CRL. Current investigations found a significant correlation of fetal demise and discrepancy in CRL at the 11th–14th week scan in monochorionic twins (13). A difference in twins’ CRL lengths <20% was usually found in twins that survived until due term, whereas when the CRL difference was >40%, a single loss was more common (14). In monochorionic twin pregnancies with a CRL discordance ≥10% the odds of birth weight discordance are three times higher than in concordant twins (8). CRL discordance at the first-trimester scan of monochorionic diamniotic twins is also considered to be a consistent early sign of twin-to-twin transfusion syndrome development in later trimesters (8,12).

A meta-analysis showed that twin pregnancies with CRL discordance ≥10% were at significantly higher risk of perinatal and fetal loss at ≥24th GW, birth weight discordance, and premature delivery before the 34th GW, but not of fetal loss before the 24th GW (15).

However, the importance of CRL discordance as a predictor of adverse outcomes has been questioned. Low sensitivity indicates that CRL discordance is not a strong predictor of twins’ demise and preterm delivery before the 34th GW (8). The reason intertwin CRL discrepancy has low sensitivity for the prediction of fetal loss might be the fact that most fetal losses in twin pregnancy are not related to first trimester growth problems, but to complications that develop in later months, such as vascular pathologies (13).

Other authors found high negative predictive value of CRL discrepancy when the CRL difference is >12% (95th percentile). In such cases, the probability of a poor outcome is 6.5% (13). However, there is no agreement regarding the cut-off value above which the perinatal outcome is unfavorably affected and the threshold ranges from 10% to 30% (16).

Our results show that having both twins live-born was not significantly correlated with the standard applied to CRL discordance of ≥10%. The reason for this might lie in the fact that there were no significant differences between the first and the second twin regarding their ultrasonographic measures in the first pregnancy trimester. Therefore, the difference in CRL length ≥10% of the longer twin was too high in our sample. The average CRL of both twins was >50 mm. Therefore, the 10% would be 5 mm. According to the ROC analysis, we determined that the required cut-off level to reliably predict the pregnancy outcome is a CRL difference between twins of 3.75 mm, which is smaller than 10%, i.e. 5 mm. This might be the reason for not achieving high sensitivity and specificity for CRL in other studies. Stricter criteria for CRL intertwin difference might be tested on larger samples in different populations.

Previous investigations also showed a higher percentage of increased NT among monochorionic diamniotic twins. Some authors have suggested that when discordance in NT between twins is 20% or more, it could be used for prediction of pregnancy complications (17,18). Still, positive and negative predictive values of NT were suboptimal. NT discordance was correlated with CRL discordance, but not with birth weight, regardless of chorionicity or sex (19).

According to our findings, twins’ Apgar scores were significantly negatively correlated with the same measures of corresponding twins’ NT. Furthermore, the NT difference was negatively correlated with twins’ birth-weight and development of pregnancy complications. Moreover, PPROM, green/bloody amniotic fluid, and pathological changes in the placenta occurred more frequently in twins with NT above the referral 95% (2 mm).
In some studies, a significant difference in placental weight between concordant and discordant twins has been observed (8). We did not register any significant differences in histopathological findings of placenta regarding the discordant twins’ growth in the first trimester.

This is the first study in which models for prediction of monochorionic diamniotic twin pregnancy outcomes were based on first-trimester ultrasonographic parameters. Results from our study show that the most important predictor of better survival of monochorionic diamniotic twins was the intertwin CRL difference, which was <3.75 mm. Moreover, preterm delivery of monochorionic diamniotic twins happened more often when CRL difference between twins was >3.75 mm. Constructed models show that the direct difference in twins’ CRL can be used to reliably predict the gestational week in which the delivery might occur. The main limitation of our study is its rather small sample size. Further testing of obtained models on more monochorionic diamniotic twins should be conducted.

In conclusion, our results suggest that first trimester measurements of CRL and NT should be taken into consideration in monochorionic diamniotic twin pregnancies, as they can imply pregnancy complications and outcomes.

References