Original Investigations

Fetal left ventricular modified myocardial performance index and renal artery pulsatility index in pregnancies with isolated oligohydramnios before 37 weeks of gestation

Madazlı et al. Fetal myocardial performance index

Hakan Erenel1, Ayşegül Özel1, Funda Öztunç2, Rıza Madazlı1

1İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Obstetrics and Gynecology, Division of Perinatal Medicine, İstanbul, Turkey
2İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Pediatrics, Division of Pediatric Cardiology, İstanbul, Turkey

Address for Correspondence: Rıza Madazlı
Phone: +90 532 613 80 81 e-mail: madazli@superonline.com


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Abstract
Objective: We aimed to evaluate fetal left modified myocardial performance index and renal artery Doppler parameter in fetuses with isolated oligohydramnios and normal amount of amniotic fluid.

Material and Methods: In a prospective cohort study, 25 pregnancies with isolated oligohydramnios and 25 healthy gestational age matched controls between 24+0 to 36+6 weeks of gestation were recruited. Primary outcome was to compare left modified myocardial performance index and mean fetal renal artery PI and secondary outcome was to compare adverse perinatal outcomes between the groups.

Results: Mean modified myocardial performance index was significantly higher and isovolumetric relaxation time was longer in the isolated oligohydramnios group (p=0.001, p=0.009). Mean renal artery PI values were not different between the groups.

Birthweight and gestational age at birth were significantly lower (p=0.041, p=0.001), and incidences of delivery before 37 weeks and Cesarean section due to non-reassuring fetal heart rate testing were significantly higher (p=0.034, p=0.021) in women with isolated oligohydramnios than the control group. We found no significant relationship between modified myocardial performance index and adverse perinatal outcomes.

Conclusion: Fetuses with isolated oligohydramnios have increased left modified myocardial performance index which may be due to mild cardiac diastolic dysfunction.

Increased modified myocardial performance index is not associated with adverse perinatal outcomes and does not seem to help in the management of pregnancies before 37 weeks of gestation with isolated oligohydramnios.

Keywords: Isolated oligohydramnios, Myocardial performance index, Perinatal outcome, Preterm, Renal artery doppler
Introduction
Amniotic fluid volume assessment is a standard part of obstetric sonography and abnormalities of the amniotic fluid volume are related to increased risk for adverse perinatal outcomes (1). An amniotic fluid index (AFI) ≤ 5 cm or a single vertical pocket of amniotic fluid ≤ 2 cm is the most common definition for oligohydramnios. Approximately 0.5% to 5% of pregnancies are complicated by oligohydramnios (2). Oligohydramnios without fetal structural and chromosomal abnormalities, intrauterine infection, uteroplacental insufficiency, premature rupture of membranes and known maternal disease is termed as isolated oligohydramnios (3). According to the literature, obstetrical outcomes of pregnancies with isolated oligohydramnios are controversial. Some studies had shown that isolated oligohydramnios is a predictor of adverse outcome (4, 5) while others have not confirmed the association (3, 6).

Fetal cardiac function can be evaluated non invasively by measuring Doppler-derived myocardial performance index (MPI) (7). Lower variability and higher inter- and intra-observer compatibility were obtained with improved modification of myocardial performance index (Mod-MPI) (8). Higher left Mod-MPI values are demonstrated to be associated with left ventricular dysfunction (9). Left Mod-MPI has been investigated in a number of complicated pregnancies to evaluate fetal cardiac dysfunction (10-12). Best to our knowledge, there is no study focusing on fetal cardiac function in isolated oligohydramnios. The main component of amniotic fluid is fetal urine in the second and third trimester. Hereby, decreased amniotic fluid can be seen secondary to impaired renal function (13). Renal arterial perfusion affects urine output directly which can be measured with renal artery Doppler parameters. However, studies focusing on alteration in renal Doppler parameters in isolated oligohydramnios showed incompatible results. According to current literature, it is difficult to state that isolated oligohydramnios is associated with renal artery Doppler parameters (14-16).

We aimed to investigate whether pregnancies before 37 weeks of gestation with isolated oligohydramnios differ in their fetal cardiac function and renal artery flow velocity waveforms from those with pregnancies with normal amniotic fluid. We also compared the outcome of pregnancies between these two groups and evaluated the value of the left Mod-MPI in the prediction of adverse perinatal outcomes.

Materials and Methods
This prospective cohort study was conducted between August 2017 and June 2018 in Istanbul University- Cerrahpasa Cerrahpasa Medical Faculty Department of Obstetrics and Gynecology Division of Perinatology. After ethical approval (Ethical committee ID: 215728), twenty-five pregnancies with isolated oligohydramnios between 24+0 to 36+6 weeks of gestation were recruited. An AFI ≤ 5 cm was defined as oligohydramnios. They were matched with 25 healthy gestational age matched singleton pregnancies with normal amniotic fluid (AFI 80-250 mm). Multiple pregnancies, preeclampsia, pregestational or gestational diabetes, other chronic diseases, premature rupture of membranes, fetal growth restriction, fetal infections, structural or chromosomal abnormalities and pathological umbilical and uterine artery Doppler indices were excluded. During the study period, Voluson E10 C4-8-D (GE Healthcare, Zipf, Austria) curved and convex array probe were used. After informed consent was obtained, detailed fetal anatomy examination was performed and AFI was calculated using the 4-quadrant method (1). In the apical four chamber view, the Doppler sample gate was kept 3 mm and located on the left wall of the ascending aorta, between the leaflets of the aortic valves (AV) and mitral valves (MV). The angle of insonation was between 0 and 300, the fastest Doppler sweep (15 cm/s) was used. Isovolumetric contraction time (ICT) was measured from MV closure to AV opening. Ejection time (ET) was measured from AV opening to closure. Isovolumetric relaxation time
(IRT) measure from AV closure to MV opening (Figure 1). The Mod-MPI was calculated as: (ICT + IRT)/ET. Three consecutive measurements were performed and the mean value was used for calculation. To evaluate renal artery blood flow, coronal plane was obtained and the Doppler gate was located on the proximal third of renal arteries (Figure 2). Angle of insonation was close to 0°. Three consecutive measurements was made for the calculation of mean left and right renal artery PI.

Pregnancies with isolated oligohydramnios were followed in every 2-3 weeks with umbilical artery Doppler until 32 weeks of gestation and every 1-2 weeks with NST and umbilical artery Doppler until 36 weeks of gestation and twice weekly thereafter. Persistently nonreactive NST was used as an indication for delivery. Labor was induced in isolated oligohydramnios cases at 39 weeks gestation if not delivered before. Pregnancies with normal amniotic fluid were followed in every four weeks until 36 weeks of gestation and examined at 38 weeks and 39 weeks of gestation and twice weekly thereafter until 41 weeks of gestation. Labor was induced at 41 weeks gestation if not delivered before. Follow-up algorithm for patients is shown in Figure 3. Route of delivery, gestational age at birth, birth weight and the presence of meconium-stained amniotic fluid in delivery were evaluated. Primary outcome was to compare left modified myocardial performance index and mean fetal renal artery PI and secondary outcome was to compare adverse perinatal outcomes between the groups. Adverse perinatal outcomes were followings situations: umbilical cord arterial pH <7.2, Apgar 5 min <7, cesarean delivery for non-reassuring fetal heart-rate testing, transient tachypnea of the newborn (TTN), respiratory distress syndrome (RDS), admission to the neonatal intensive care unit (NICU) and hypoxic ischemic encephalopathy (HIE), and neonatal death.

Statistical Analysis
Statistical analysis was made with SPSS v20.0 software. Categorical data were analysed using the Chi square test or Fisher’s exact test. Numerical variables were compared using Student’s t-test or Mann–Whitney U. Pearson’s rank correlation was studied between MPI and adverse perinatal outcomes. Pearson correlation coefficient (r) was used. A p-value less than 0.05 and r higher than 0.5 were considered to be statistically significant.

Results
The clinical characteristics of pregnancies with isolated oligohydramnios and normal amniotic fluid are illustrated in Table 1. Maternal age and nulliparity showed no difference. Gestational age at ultrasound and umbilical artery PI values were similar among the two groups (p>0.05). Mean AFI was 31 and 109 mm in the isolated oligohydramnios and control group, respectively (p<0.001).

Cardiac and renal artery Doppler parameters of pregnancies with isolated oligohydramnios and control group are presented in Table 2. Mean Mod-MPI value was significantly higher and IRT was longer in the isolated oligohydramnios group than the control group (p=0.001, p=0.009). Mean ICT, ET values and mean renal artery PI value were not significantly different between the isolated oligohydramnios and control group (p>0.05). Perinatal outcomes in the isolated oligohydramnios and control group are presented in Table 3. Gestational age at birth and birth weight were significantly lower (p=0.041, p=0.001), and incidences of delivery before 37 weeks and cesarean section due to non-reassuring fetal heart rate testing were significantly higher (p=0.034, p=0.021) in women with isolated oligohydramnios than the control group. Incidences of labor induction, arterial cord pH<7.2, Apgar 5 min<7, meconium stained amniotic fluid, admission to NICU, transient tachypnea of the newborn, hypoxic ischemic encephalopathy, respiratory distress syndrome and neonatal death were not significantly different between the pregnancies with isolated oligohydramnios
and normal amniotic fluid (p>0.05). Preterm induction of labor was performed in two patients with isolated oligohydramnios due to nonreassuring fetal heart rate (36-37 weeks). There was no significant correlation between Mod-MPI values and adverse perinatal outcomes (Pearson’s r=0.112, p=0.440).

**Discussion**

In the current study, we have observed that isolated oligohydramnios before 37 weeks were characterized by a higher rate of preterm delivery and a higher rate of cesarean delivery for non-reassuring fetal heart rate testing during labor. However, adverse perinatal outcomes such as arterial cord pH<7.2, Apgar 5 min<7, meconium-stained amniotic fluid, admission to NICU and neonatal death were not significantly different between the pregnancies with isolated oligohydramnios and normal amniotic fluid. Although we observed higher rate of preterm delivery in the isolated oligohydramnios, the neonatal morbidity was similar. One possible explanation for this discrepancy might be higher rate of late preterm deliveries at a gestational age of 36-37 weeks. Although it has been reported that isolated oligohydramnios at preterm pregnancy is associated with higher rate of adverse neonatal outcomes, subgroup analysis showed that adverse outcomes were substantially related to the induction of delivery but not to the isolated oligohydramnios itself (6). Melamed et al. showed that the neonatal outcome in the isolated oligohydramnios group (expectant-management) was similar to that observed in the control group (6).

A recent meta-analysis including 6 studies of isolated oligohydramnios in 27,526 women showed that pregnancies with isolated oligohydramnios had significantly higher rates of meconium aspiration syndrome, cesarean delivery for fetal distress and admission to the NICU. It has been concluded that isolated oligohydramnios is a pathological finding and there are not sufficient data to determine the optimal timing of delivery to reduce the risk of adverse outcomes (5). Several other studies have reported that perinatal outcomes in pregnancies with isolated oligohydramnios were similar to pregnancies with normal amniotic fluid (17, 18). Our findings support the results of studies demonstrating isolated oligohydramnios is not significantly associated with adverse perinatal outcome (6, 17, 18).

The amount of amniotic fluid depends on renal filtration and urine production. Renal artery Doppler velocimetric parameters reflect the arterial perfusion of the kidneys and these parameters may be related to amniotic fluid level. Several studies aimed to investigate the relationship between fetal renal artery Doppler parameters and amniotic fluid level however these studies showed inconsistent results (14, 15, 19, 20). Yoshimura et al. showed that renal artery pulsatility index is significantly higher in pregnancies with isolated oligohydramnios compared to pregnancies with normal amniotic fluid (20). In another study including 63 pregnancies followed from 16 to 41 weeks found no correlation between amniotic fluid levels and fetal renal artery pulsatility index (14). Benzer et al. evaluated renal artery pulsatility index in pregnancies with oligohydramnios at 22, 28 and 34 weeks of gestation and found significantly higher renal artery pulsatility index only at 28 weeks of gestation but not at 22 or 34 weeks (15). Budunoglu et al. reported that renal artery pulsatility index was not significantly different between patients with isolated oligohydramnios and normal amniotic fluid at 25 to 40 weeks of gestation (16). In the current study, renal artery pulsatility index was not significantly different between pregnancies before 37 weeks of gestation with isolated oligohydramnios and normal amniotic fluid, suggesting that isolated oligohydramnios may not be related with impaired renal artery blood flow. Mod-MPI values are associated with fetal left ventricular function and it has become a reliable marker of fetal cardiac dysfunction. Fetal MPI has been evaluated in several high risk pregnancies such as diabetic and postterm pregnancies, fetal growth restriction and twin-twin transfusion syndrome (12, 21, 22).
We evaluated modified myocardial performance index in pregnancies with isolated oligohydramnios and demonstrated subtle cardiac dysfunction in fetuses with isolated oligohydramnios compared with healthy controls. The higher Mod-MPI levels have been found to be primarily due to an elevated IRT. IRT becomes abnormal in the initial stages of cardiac dysfunction and is mainly caused by decreased diastolic compliance (23). Calcium reuptake of myocardial cells are reduced, which leads to prolongation of complete cardiomyocytes relaxation and an increased IRT (24). According to the findings of the present study, we may speculate that there may be a mild diastolic dysfunction in fetuses with isolated oligohydramnios. However, whether oligohydramnios by itself is the cause or the consequence of mild diastolic dysfunction is not clear. There is only one study that evaluated the association between increased amount of amniotic fluid and Mod-MPI in pregnancies with isolated polyhydramnios. In that study, Mod-MPI was significantly higher in isolated polyhydramnios compared with controls and Mod-MPI was also associated with adverse perinatal outcome (25). However, we could not demonstrate any association between Mod-MPI values and adverse perinatal outcomes in fetuses with isolated oligohydramnios. Our study suggests that Mod-MPI evaluation does not seem to help in the management of pregnancies before 37 weeks of gestation with isolated oligohydramnios. The strength of this study was its prospective design and measurement of Doppler parameters by 1 experienced examiner. However, the limitation of the study was the small sample size.

Conclusion
In conclusion, fetuses with isolated oligohydramnios have increased Mod-MPI may be due to mild fetal cardiac diastolic dysfunction. Increased Mod-MPI was not associated with adverse perinatal outcomes in fetuses with isolated oligohydramnios. Further large studies are needed to investigate the importance of Mod-MPI in isolated oligohydramnios.

Statement of Ethics: Ethical approval was obtained

Disclosure Statement: There are no conflict of interest

References

Table 1. The clinical characteristics of pregnancies with isolated oligohydramnios and control group

<table>
<thead>
<tr>
<th>Isolated Oligohydramnios</th>
<th>Control group</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Maternal age (years)</td>
<td>30.6±6.3</td>
<td>29.8±5.4</td>
</tr>
<tr>
<td>Nulliparity</td>
<td>14(56)</td>
<td>12(48)</td>
</tr>
<tr>
<td>Gestational age at ultrasound (weeks)</td>
<td>30.2 ± 4.8</td>
<td>30 ± 5</td>
</tr>
<tr>
<td>Mean AFI (mm)</td>
<td>31 (21-46)</td>
<td>109 (90-140)</td>
</tr>
<tr>
<td>Umbilical artery PI</td>
<td>0.99 ±0.14</td>
<td>0.99 ± 0.17</td>
</tr>
</tbody>
</table>

Data are presented as mean± SD or n(%)  
* \( p \) value of< 0.05
Table 2. Cardiac and renal artery Doppler parameters of pregnancies with isolated oligohydramnios and control group

<table>
<thead>
<tr>
<th>Isolated</th>
<th>Control</th>
<th>( p ) value oligohydramnios</th>
<th>group</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>25</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Modified myocardial performance index</td>
<td>0.53 ± 0.11</td>
<td>0.43 ± 0.08</td>
<td>0.001*</td>
</tr>
<tr>
<td>Isovolumetric contraction time (ms)</td>
<td>36.6 ± 0.9</td>
<td>32.1 ± 0.7</td>
<td>0.069</td>
</tr>
<tr>
<td>Ejection time (ms)</td>
<td>161.7 ± 19.4</td>
<td>169.8 ± 10.9</td>
<td>0.074</td>
</tr>
<tr>
<td>Isovolumetric relaxation time (ms)</td>
<td>48.6 ± 1.0</td>
<td>41.2 ± 0.9</td>
<td>0.009*</td>
</tr>
<tr>
<td>Mean renal artery PI</td>
<td>2.31 ± 0.41</td>
<td>2.31 ± 0.23</td>
<td>0.995</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD

*p value of< 0.05

Table 3. Perinatal outcomes in the isolated oligohydramnios and control group

<table>
<thead>
<tr>
<th>Isolated</th>
<th>Control</th>
<th>( p ) value oligohydramnios</th>
<th>group</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>25</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Gestational age at birth (weeks)</td>
<td>36.9 ± 2.7</td>
<td>38.4 ± 2.1</td>
<td>0.041*</td>
</tr>
<tr>
<td>&lt;37 weeks</td>
<td>8(32)</td>
<td>2(8)</td>
<td>0.034*</td>
</tr>
<tr>
<td>&lt;34 weeks</td>
<td>2(8)</td>
<td>1(4)</td>
<td>0.552</td>
</tr>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>p value</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------</td>
<td>-----------</td>
<td>---------</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>2660 ± 570</td>
<td>3199 ± 464</td>
<td>0.001*</td>
</tr>
<tr>
<td>Labor induction</td>
<td>6(24)</td>
<td>2(8)</td>
<td>0.123</td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>14(56)</td>
<td>7(28)</td>
<td>0.045*</td>
</tr>
<tr>
<td>Nonreassuring fetal heart rate</td>
<td>7(28)</td>
<td>1(4)</td>
<td>0.021*</td>
</tr>
<tr>
<td>Meconium-stained amniotic fluid</td>
<td>0</td>
<td>0</td>
<td>N/A</td>
</tr>
<tr>
<td>Arterial cord pH&lt;7.2</td>
<td>0</td>
<td>0</td>
<td>N/A</td>
</tr>
<tr>
<td>5-min Apgar score &lt; 7</td>
<td>3(12)</td>
<td>0</td>
<td>0.07</td>
</tr>
<tr>
<td>Neonatal intensive care unit admission</td>
<td>4(16)</td>
<td>1(4)</td>
<td>0.157</td>
</tr>
<tr>
<td>Transient tachypnea of the newborn</td>
<td>2</td>
<td>0</td>
<td>0.149</td>
</tr>
<tr>
<td>Respiratory distress syndrome</td>
<td>2</td>
<td>1</td>
<td>0.552</td>
</tr>
<tr>
<td>Hypoxic ischemic encephalopathy</td>
<td>0</td>
<td>0</td>
<td>N/A</td>
</tr>
<tr>
<td>Neonatal death</td>
<td>0</td>
<td>0</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Data are presented as mean± SD or n(%)
N/A, not applicable *p value of< 0.05

**Figure 1.** Measurement of fetal left ventricle myocardial performance index
Figure 2. Measurement of fetal renal artery Doppler
**Figure 3.** Follow-up algorithm for patients

- **Diagnosis of isolated oligohydramnios was made after 24 weeks of gestation**
  - N=25
  - Unilateral artery Doppler and growth scan every 2-3 weeks
  - NST and umbilical artery Doppler every 1-2 weeks fortnightly growth scan
  - Twice weekly NST and umbilical artery Doppler fortnightly growth scan
  - Labor induction at 39 weeks gestation
    - Labor induction before 39 weeks of gestation due to persistently nonreactive NST
- **Pregnancies with normal amniotic fluid**
  - N=25
  - Monthly growth scan
  - NST and umbilical artery Doppler and growth scan
  - NST and amniotic fluid volume assessment
  - Twice weekly NST and amniotic fluid volume
  - Labor induction at 41 weeks of gestation
    - Labor induction before 41 weeks of gestation due to persistently nonreactive NST