Assessment of Fetal Myocardial Performance Index in Women with Placenta Previa

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Background: This study investigated whether fetuses of placenta previa pregnancies have cardiac dysfunction by use of a modified myocardial performance index (Mod-MPI).

Material/Methods: A prospective cross-sectional study was conducted including 178 fetuses at 28–40 weeks of gestation. Eighty-nine fetuses of mothers with placenta previa and without pregnancy complications were recruited (placenta previa group) and matched with 89 fetuses of mothers with normal pregnancies (control group). Fetal cardiac function parameters and perinatal outcomes as well as the Mod-MPI were compared between the 2 groups.

Results: The median Mod-MPI was significantly increased in fetuses of mothers with placenta previa compared with controls (0.47±0.05 vs. 0.45±0.05; P<0.01). Among fetuses of mothers with or without placenta previa, the Mod-MPI was significantly higher in the incomplete placenta previa group compared with the complete placenta previa group and control group (P<0.01). An increased Mod-MPI in placenta previa pregnancies was independently associated with fetal cord pH <7.2 (odds ratio, 4.8; 95% confidence interval, 0.98–23.54; P=0.003).

Conclusions: There is impairment of fetal cardiac function in pregnancies with placenta previa. An increased MPI was independently associated with adverse perinatal outcomes to some extent in the placenta previa pregnancies.

MeSH Keywords: Echocardiography, Doppler • Fetal Heart • Placental Circulation

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Background

With the opening of the two-child policy in mainland China, the incidence of placenta previa is increasing. The overall prevalence of placenta previa is approximately 1.24% in mainland China [1]. Because of the possibility of obstetric hemorrhage, placenta previa has been reported to be related to adverse fetomaternal outcomes [2–4]. A possible etiology of placenta previa is poor placentation leading to placental dysfunction with reduced placental perfusion [5–7]. The heart plays a central role in the fetal adaptive mechanism to placental insufficiency and hypoxia. Animal studies have demonstrated that placental insufficiency may lead to decreased maturation and proliferation of fetal cardiomyocytes [8,9]. In addition, human studies have shown an association of poor placental function with cardiovascular diseases in later life [10,11]. However, the effect of placenta previa on fetal heart functions has not been investigated systematically.

Accurate ultrasound assessment of fetal cardiac functions is of great importance in fetal medicine research. Early detection of subtle changes in myocardial motion could be potentially lifesaving and useful for timing the delivery properly. New ultrasound techniques [12,13] have been applied to overcome the limitations of conventional two-dimensional imaging and M-mode techniques. One of them is the myocardial performance index (MPI), a non-invasive Doppler-derived technique that evaluates global myocardial function [14]. The MPI has proven to be a reliable indicator of fetal cardiac dysfunction that reflects early cardiac adaptation to intrauterine insults [15]. An increased MPI suggesting fetal cardiac dysfunction has been demonstrated to be an indicator of adverse outcomes in a number of pathological conditions such as gestational diabetes, growth restriction, and pre-eclampsia [16–18]. However, the technology has evolved to include modification of the myocardial performance index (Mod-MPI), which is associated with lower differentiation and higher inter- and intra-observer consistency than is the MPI.

The aim of our study was to investigate fetal cardiac function by use of the Mod-MPI in placenta previa pregnancies and to evaluate whether this parameter is linked to adverse perinatal outcomes in placenta previa pregnancies.

Material and Methods

Patients

A prospective, cross-sectional study was conducted with the approval of the Institutional Review Board (IRB) of Beijing Obstetrics and Gynecology Hospital Affiliated to Capital Medical University. All pregnant women had provided written informed consent. Eighty-nine singleton pregnant women diagnosed with placenta previa at 28–40 weeks of gestation were recruited to the study from November 2015 to February 2017. They were matched with 89 healthy women with normal pregnancies. Exclusion criteria were: intrauterine growth restriction, congenital malformations, abnormal fetal heart rates, multiple pregnancies, chromosomal anomalies, pregnancy complications (e.g., pre-eclampsia), hypertension, diabetes mellitus, and drug use. Placenta previa was defined as placenta tissue covering all or part of the internal os, which was confirmed by transabdominal ultrasound at 28–40 weeks of gestation.

Ultrasound examination

Fetal echocardiography was conducted in each pregnant woman by using the Samsung WS80A ultrasound system (Medison, Korea). The Mod-MPI of the fetal left ventricle was estimated as originally described by Hernandez-Andrade et al. [19] (Figures 1, 2). A cross-sectional view of a cardiac apical 4-chamber image was acquired. The Doppler sample was located at the medial wall of the ascending aorta, which included the leaflet of...
the mitral valve (MV) and aortic valve (AV). Opening and closing of MV and AV clicks were imaged. The angle of insonation was <30°. The Doppler gain was lowered enough to identify the echoes clearly marking the opening and closing of the MV and AV clicks. The Doppler sweep speed was set at 540 Hz, scale at 55 cm/s, and wall motion filter at 100 Hz. The following 3 periods were calculated: isovolumic contraction time (ICT) was from MV closure to AV opening, isovolumic relaxation time (IRT) was from AV closure to MV opening, and ejection time (ET) was from AV opening to closure. Therefore, the Mod-MPI=(ICT+IRT)/ET.

Fetal biometric measurements included biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL), and estimated fetal weight (EFW) was estimated. Doppler waveform and fetal echocardiography were performed as described by the International Society of Ultrasound in Obstetrics and Gynecology Practice Guidelines [20]. E wave (early ventricular filling) and A wave (active atrial filling) peak velocities, and the E/A ratio of the MV and TV were calculated in apical 4-chamber images by Doppler sample placing at the tip of the 2 valves during diastole (Figures 3–6). In addition, the pulsatility index (PI) of the umbilical artery (UA) was measured in a free loop of cord away from fetal insertion or placental insertion sites (Figures 7, 8). The pulsatility index (PI) of the middle cerebral artery (MCA) was measured at the proximal third of the artery, where it is near the MCA origin in the internal carotid artery. Color flow mapping was applied to identify Willis’ circle. The insonation angle was adjusted as far as possible to 0° (Figures 9, 10). The PI of the ductus venosus (DV) was calculated from a mid-sagittal view of the fetal trunk. Color flow mapping was applied to identify a standard sampling site with high velocity at its narrow entrance (Figures 11, 12).

The cerebroplacental ratio(MCA/UA-PI) was calculated by dividing the MCA pulsatility index by the UA pulsatility index.

Placental size and perinatal consequences

After delivery, untrimmed placentas attached to the membranes and umbilical cord were immediately weighed. Placental size was measured, and the placenta-to-birth weight ratio (PW/BW) and placental volume were estimated and recorded.
Neonatal and maternal outcomes were defined by any 1 of the following: prematurity, stillbirth, neonatal intensive care unit admission, respiratory distress, intraventricular hemorrhage, hypoglycemia, metabolic acidosis, cord pH <7.2, maternal moderate and severe anemia, hysterectomy, and blood transfusion.

We further investigated the relationship between an elevated MPI and adverse pregnancy outcomes in the placenta previa group by dividing them into MPI of below or above the 95th percentile in terms of the nomogram as described previously [21].

Figure 7. Ultrasound Doppler spectrum of fetal UA in the control group.

Figure 8. Ultrasound Doppler spectrum of fetal UA in the placenta previa group.

Figure 9. Ultrasound Doppler spectrum of fetal MCA in the control group.

Figure 10. Ultrasound Doppler spectrum of fetal MCA in the placenta previa group.

Figure 11. Ultrasound Doppler spectrum of fetal DV in the control group.

Figure 12. Ultrasound Doppler spectrum of fetal DV in the placenta previa group.
Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, version 22.0 for Windows). Comparisons of continuous variables between 2 groups were performed by the independent-samples t test. Categorical data were analyzed by χ² test. Frequencies in the groups with a MPI below and above the 95th percentile were compared by the χ² test. Post hoc test results among the control group, the CPP group, and the ICP group were compared by the Bonferroni test. A value of P<0.05 was considered as statistically significant.

Results

The clinical characteristics of the 2 groups are shown in Table 1. The 2 groups were similar in terms of body mass index, gestational age at admission, fetal sonographic biometry, estimated fetal weight (EFW), DV-PI, and MCA/UA-PI. MCA and UA-PI values were lower in the placenta previa group than in the control group (Table 1). In addition, parturients were older with a higher placental weight, thicker placenta, and higher placental-to-birth weight ratio compared with the control group (Table 2). The Bonferroni post hoc test showed that the Mod-MPI values

| Table 1. Clinical characteristics of the two groups. |
|---------------------------------|-----------------|----------------|
|                                 | Control (n=89)  | Placenta previa (n=89) | p Value |
| Maternal age (week)            | 29.3±2.8        | 32.5±3.6          | <0.001  |
| BMI (kg/m²)                    | 26.9±2.6        | 26.8±3.14         | 0.915   |
| Gestational age (week)         | 33.5±2.6        | 33.7±2.6          | 0.434   |
| BPD                            | 8.4±1.1         | 8.3±0.7           | 0.549   |
| HC                             | 30.5±2.0        | 30.9±2.2          | 0.260   |
| AC                             | 29.3±2.9        | 30.3±2.8          | 0.220   |
| FL                             | 6.5±0.6         | 6.6±0.6           | 0.278   |
| EFW (g)                        | 2403.1±612.4    | 2273.2±602.8      | 0.153   |
| Gestational age at birth (weeks)| 39.0±1.0       | 37.3±1.6          | <0.001  |
| Birth weight (g)               | 3380.2±367.2    | 3166.2±419.8      | <0.001  |
| Birth size (cm)                | 50.3±10.9       | 49.4±2.3          | 0.007   |
| Male                           | 42 (46.2%)      | 43 (48.3%)        | 0.720   |
| UA-PI                          | 0.88±0.11       | 0.84±0.15         | 0.036   |
| MCA-PI                         | 1.88±0.56       | 1.72±0.41         | 0.036   |
| MCA/UA-PI                      | 2.10±0.60       | 2.15±0.63         | 0.616   |
| DV-PI                          | 0.51±0.20       | 0.53±0.17         | 0.419   |

Table 2. Placental size in pregnancies with and without placenta previa.

|                                 | Control (n=89)  | Placenta previa (n=89) | p Value |
| Weight (g)                      | 583.01±121.99   | 681.24±140.16          | <0.001  |
| Placenta-to-birth weight ratio  | 0.17±0.03       | 0.21±0.04              | <0.001  |
| Maximal diameter (cm)           | 19.68±1.4       | 20.66±3.0              | 0.007   |
| Lesser diameter (cm)            | 18.34±1.7       | 18.31±2.3              | 0.939   |
| Thickness (cm)                  | 2.17±0.46       | 2.50±0.49              | <0.001  |
| Volume (cm³)                    | 411.90±108.17   | 489.19±144.14          | <0.001  |
in the incomplete placenta previa group were significantly higher than those in the incomplete placenta previa and control groups. There were no significant differences in Mod-MPI values between complete placenta previa and control groups (Table 3).

Routine echocardiographic parameters are shown in Table 4. The E wave, A wave peak velocity, and E/A ratios of the mitral valve were similar between the 2 groups. The mean tricuspid valve E wave and A wave velocities were found to be significantly lower in the placenta previa group than in the control group; however, there was no difference in the tricuspid valve E/A ratio between the groups. The fetal MPI was higher in the placenta previa group than in the control group. ICT and ET were similar in the 2 groups, while IRT was significantly longer in fetuses of the placenta previa group compared with the control group. Table 5 shows Doppler and cardiac parameters of the placenta previa group as Z scores, percentages for 5th and 95th percentiles, and mean values.

To evaluate the relationship between adverse fetomaternal outcomes and the MPI, the 89 cases with placenta previa were divided into 2 groups with a normal (<95th percentile) or elevated (≥95th percentile) MPI in fetuses (Table 6). An elevated MPI in placenta previa pregnancies was independently associated with fetal cord pH <7.2 (odds ratio, 4.8; 95% confidence interval, 0.98–23.54; P=0.003).

Table 3. The Bonferroni post-hoc tests.

| Dependent variable | Multiple comparisons | 95% Confidence interval |
|--------------------|----------------------|-------------------------|
|                    | Mean difference (I-J) | Std. error | Sig | Lower bound | Upper bound |
| Mod-MPI            |                       |            |     |             |             |
| Control            | -0.012670             | 0.00832    | 0.130 | -0.0291 | 0.0037 |
| CPP                | -0.03082*             | 0.00919    | 0.001 | -0.0490 | -0.0127 |
| ICP                |                      |            |     |             |             |
| Control            | 0.01267               | 0.00832    | 0.130 | -0.0037 | 0.0291 |
| CPP                | -0.01815              | 0.01021    | 0.077 | -0.0383 | 0.0020 |
| ICP                | 0.03082*              | 0.00919    | 0.001 | 0.0127 | 0.0490 |
| CCP                | 0.01815               | 0.01021    | 0.077 | -0.0020 | 0.0383 |

Mod-MPI – modified myocardial performance index; CPP – complete placenta previa; ICP – incomplete placenta previa. * The mean difference is significant at the 0.05 level.

Table 4. Cardiac function parameters in two groups.

|                  | Control (n=89) | Placenta previa (n=89) | p Value |
|------------------|--------------|------------------------|---------|
| Heart rate (beats/min) | 145.64±11.1   | 145.02±9.6             | 0.692   |
| TV E velocity (cm/s)   | 44.57±10.05   | 39.61±9.92             | 0.001   |
| TV A velocity (cm/s)   | 61.88±10.26   | 57.34±9.71             | 0.003   |
| TV E/A               | 0.72±0.11     | 0.69±0.11              | 0.088   |
| MV E velocity (cm/s)   | 36.57±7.61    | 35.92±6.81             | 0.547   |
| MV A velocity (cm/s)   | 52.72±8.62    | 51.11±7.30             | 0.177   |
| MV E/A               | 0.70±0.10     | 0.71±0.12              | 0.502   |
| MPI (ms)             | 0.45±0.05     | 0.47±0.05              | 0.005   |
| IRT (ms)             | 41.64±6.40    | 45.35±6.76             | <0.001  |
| ICT (ms)             | 33.17±7.93    | 35.27±6.79             | 0.058   |
| ET (ms)              | 168.41±14.22  | 171.42±14.47           | 0.161   |

Data are presented as mean ±SD.
### Table 5. Z Scores and percentages for 5th percentile, mean, and 95th percentile values of Doppler and cardiac parameters in the placenta previa group.

| Parameter          | Z Score | 5th percentile | Mean | 95th percentile | 5th percentile | Mean | 95th percentile |
|--------------------|---------|----------------|------|-----------------|----------------|------|-----------------|
| UA-PI              | −2.62   | −0.47          | 1.95 | 91.00           | 36.00          | 9.0  |
| MCA-PI             | −1.55   | −0.19          | 0.98 | 89.80           | 38.60          | 4.50 |
| MCA/UA-PI          | −1.40   | −0.16          | 1.68 | 87.50           | 45.40          | 4.50 |
| Heart rate         | −1.44   | −0.06          | 1.42 | 95.50           | 48.30          | 1.10 |
| TV E velocity      | −1.89   | −0.73          | 1.28 | 82.02           | 34.83          | 3.37 |
| TV A velocity      | −2.03   | −0.49          | 1.39 | 87.64           | 31.46          | 2.25 |
| TV E/A             | −1.65   | −0.45          | 2.00 | 94.38           | 38.20          | 4.49 |
| MV E velocity      | −1.62   | −0.04          | 1.47 | 91.01           | 46.07          | 1.12 |
| MV A velocity      | −1.57   | −0.17          | 1.29 | 97.75           | 47.19          | 0.00 |
| MV E/A             | −1.53   | −0.02          | 1.83 | 95.51           | 44.94          | 7.87 |
| MPI                | −1.41   | 0.52           | 2.01 | 98.90           | 67.40          | 9.00 |
| IRT                | −1.04   | 0.68           | 2.46 | 96.60           | 77.50          | 16.90|
| ICT                | −0.99   | 0.23           | 1.96 | 98.90           | 70.80          | 4.50 |
| ET                 | −1.39   | 0.04           | 1.83 | 97.80           | 55.10          | 3.40 |

### Table 6. Perinatal outcomes of the placenta previa group in terms of the fetal myocardial performance index.

| Parameter                              | MPI <95th percentile (n=81) | MPI >95th percentile (n=8) | p Value |
|----------------------------------------|------------------------------|---------------------------|---------|
|                                        | n               | %             | n      | %             |         |
| Obstetric                              |                 |               |        |               |         |
| Maternal moderate and severe anemia    | 8               | 9.9           | 1      | 12.5          | 0.814   |
| Hysterectomy                           | 7               | 8.6           | 0      | 0             | 0.386   |
| Blood transfusion                      | 10              | 12.3          | 1      | 12.5          | 0.990   |
| Prematurity                            | 21              | 25.9          | 3      | 37.5          | 0.495   |
| Stillbirth                             | 1               | 1.2           | 0      | 0             | 0.752   |
| Neonatal                               |                 |               |        |               |         |
| NICU admission                         | 20              | 24.7          | 3      | 37.5          | 0.430   |
| Hypoglycemia                           | 12              | 14.8          | 1      | 12.5          | 0.860   |
| Intraventricular hemorrhage            | 3               | 3.7           | 0      | 0             | 0.580   |
| Respiratory distress                   | 3               | 3.7           | 0      | 0             | 0.580   |
| Metabolic acidosis                     | 0               | 0             | 1      | 12.5          | 0.001   |
| Cord pH < 7.2                          | 9               | 11.1          | 3      | 37.5          | 0.037   |
Discussion

The results of the present study suggest that fetuses of mothers with placenta previa have impairment of cardiac function, as shown by significantly higher MPI values compared with controls. Increased MPI in placenta previa pregnancies was independently associated with adverse perinatal outcomes to some extent.

Several perinatal conditions have a considerable effect on fetal cardiac function. The leading causes of fetal cardiovascular deterioration in growth-restricted fetuses are increased placental vascular resistance, followed by increased cardiac afterload [22]. In fetuses of mothers with pre-eclampsia, increased placental vascular resistance can lead to an increased MPI [18,23]. Placental bed biopsies have revealed that placenta previa is associated with higher trophoblastic giant cell infiltration and increased placental vascular supply lesions [7]. Stereological analysis of placenta previa has shown increased blood vessels of chorionic villi and a reduction in the villous surface fibrin volume [6]. All of these factors may finally result in placental dysfunction [6] and consequently an increased cardiac afterload. Our findings suggest a larger placenta and higher placental-to-birth weight ratio in placenta previa pregnancies, which are usually indicative of placental dysfunction at all gestational ages [24,25]. The likely explanation for this finding is that an inappropriately heavy placenta can reduce the placental transport ability to sustain fetal growth [24]. A thicker placenta may be less efficient because of an increased villous depth and decreased blood perfusion, which likely increase fetal energy expenditure and cardiovascular resistance [25], thereby increasing cardiac afterload and cardiac dysfunction.

Ventricular malfunction is associated with increased MPI values [26], usually due to an elevated IRT. IRT becomes abnormal in the initial stages of cardiac dysfunction [27,28] as the main parameter. Calcium reuptake of myocardial cells are reduced, which can lead to prolongation of complete cardiomyocytes relaxation and an increased IRT [29]. A prolonged IRT frequently accompanies a shortened ET, while the ICT is the steadiest [15]. The unchanged ET in our study was expected because other studies have shown that ET may be steady in complicated pregnancies when IRT is increased [28,30]. It has been reported that reference left ventricular MPI values have a wide range of variation. MPI values of 0.35, 0.41, and 0.53 with no changes during gestation have been reported in normal fetuses [26,31,32]. Tsutsumi et al. [33] reported a gradual decrease in MPI of both ventricles throughout pregnancy. Conversely, Hernandez-Andrade et al. [19] reported a small increase at 19 to 39 weeks of gestation. In the present study, the MPI values were 0.45 and 0.47 in the control group and placenta previa group, respectively. The mean MPI value of the control group in our study was within normal limits, as demonstrated by other studies [19,32,33]. However, to the best of our knowledge, the present study is the first to assess the use of the MPI in routine ultrasound scans of placenta previa pregnancies.

Because the aim of this study was to investigate the effects of placenta previa on fetal blood circulation, we also examined the UA and MCA blood flows. Interestingly, fetuses of mothers with placenta previa had significantly lower UA and MCA pulsatility indexes; the former was likely due to superficial implantation of the placenta and deep infiltration of trophoblasts. The supply of blood and oxygen is greater when the placenta is implanted in the lower uterine segment rather than in the upper segment. Thus, hypoxemia can be improved and vascular remodeling can occur more easily [34,35]. Complete placenta previa often occurs with concurrent placenta accrete, and trophoblasts implant more deeply [36,37], which can contribute to more blood flow to the intervillous space. Combined with an increased MPI, we speculate that impaired placental function might not fundamentally improve, although placental factors might play a protective role in placenta previa pregnancies. The mean MCA-PI in the placenta previa group was not as low as 2 SD below the mean for gestational age, indicating no reason to suspect a brain-sparing effect in these fetuses.

It is well known that placenta previa is a severe pregnancy complication that can be associated with adverse pregnancy outcomes. Furthermore, our study has shown that fetuses of mothers with placenta previa and an MPI above the 95th percentile had an elevated risk of fetal cord pH <7.2. An increased MPI in placenta previa pregnancies was independently associated with fetal cord pH <7.2 (odds ratio, 4.8; 95% confidence interval, 0.98–23.54; P=0.003). Adverse fetal outcomes might be explained by a combination of placenta previa, prematurity, placental malfunction, and cardiac dysfunction. Impairment of cardiac function would thus to some extent be an extra risk factor for adverse outcome of fetuses in the placenta previa group.

The MPI has been demonstrated to be a marker to evaluate cardiac functions of both ventricles. Because the fetal right heart dominates in fetal circulation [38,39], assessment of the right ventricle can reveal some early findings of cardiac dysfunction. However, MPI evaluation of the right ventricular needs to acquire a two-plane image and capture the pulmonary and tricuspid valves waveforms, which makes right heart assessment difficult. However, as the characteristic anatomy of the left heart, the flows of the aorta and mitral valves can be easily investigated in the same Doppler image. Thus, we prefer to acquire left ventricular MPI rather than right ventricular MPI because of left heart advantages and right heart complexity. We found no differences in left cardiac parameters between the 2 groups except for the MPI value. Reduced E/A ratios are beneficial to evaluate fetal compromise [40,41], but changes in the E/A ratio are linked to severe Doppler flow.
worsening [42]. The normal E/A ratios and prolonged MPI in our
study also demonstrate that MPI is a more sensitive indicator
than other cardiac parameters in placenta previa pregnancies.

To the best of our knowledge, this is the first study to assess
fetal left ventricular MPI in a placenta previa group. A limitation
of this study is the small sample size of fetuses of mothers with
placenta previa. Thus, a longitudinal study with a larger sam-
ple size of fetuses in placenta previa pregnancies is warranted.

Conclusions

To conclude, this is a preliminary study that demonstrated im-
pairment of fetal cardiac function by means of the left ventric-
ular Mod-MPI in pregnancies with placenta previa. An increased
Mod-MPI in pregnancies with placenta previa was independent-
ly associated with adverse perinatal outcomes to some extent.
Hence, measurement of the fetal Mod-MPI is very important
for the management of placenta previa pregnancies. A future
multicenter prospective study may demonstrate the clinical
utility of Mod-MPI in placenta previa pregnancies. If verified,
the Mod-MPI may become an additional parameter to be in-
tegrated into daily fetal ultrasound scanning to recognize pos-
sible fetal distress in placenta previa pregnancies. Our study
shows that identification of an increased Mod-MPI in fetuses
can assist clinicians to make decisions regarding hospitaliza-
tion, close monitoring, and timing of delivery.

Conflicts of interests

None.

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