Velocity vector imaging for evaluation of fetal vertical function throughout gestation

Noriko Natori1, Rie Oyama1, Tsukasa Baba1, Chizuko Isurugi1, Hideyuki Chida1,2, Gen Haba1, Yuri Sasaki1, Tomonobu Kanasugi1,3, Hiroaki Itamochi1, Akihiko Kikuchi1,4

1Department of Obstetrics and Gynecology, Iwate Medical University School of Medicine, Shiwa, Iwate, Japan, 2Department of Obstetrics and Gynecology, Iwate Prefectural Ninohe Hospital, Ninohe, Japan, 3Department of Obstetrics and Gynecology, Iwate Prefectural Ofunato Hospital, Ofunato, Japan, 4Center for Maternal, Fetal and Neonatal Medicine, Department of Obstetrics and Gynecology, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan

Aim: Velocity vector imaging (VVI) is a speckle-tracking ultrasonographic assessment technique used to evaluate myocardial function. However, VVI values show wide deviations. This study aimed to clarify the significance of serial VVI values for assessing fetal cardiac function.

Methods: Echocardiographic images of 50 fetuses (normal: n = 29, fetal growth restriction [FGR]: n = 21) were obtained in the four-chamber view during the second and third trimester. VVI images were analyzed for longitudinal velocity, strain, and strain rate in the global and segmental walls of the left ventricle (LV) and right ventricle (RV).

Results: Global longitudinal velocity (GLV) of the LV and RV during the third trimester did not significantly differ between FGR and normal fetuses. LVd and RVs appeared to be low in HDP cases, although there were no significant differences compared to no HDP cases. Eighty-two serial images obtained from 13 normal singleton fetuses revealed increased systolic GLV of the LV and RV, increased diastolic GLV in 10 cases, and increased longitudinal velocity in the basal and middle free wall of both the LV and RV.

Conclusions: The evaluation of fetal ventricular function using VVI revealed that GLV increases throughout gestation.

Introduction

Fetal cardiac physiology has been assessed by ultrasonography for the past 35 years, as it is non-invasive and provides real-time information on fetal cardiac function. Velocity vector imaging (VVI) is a new modality that allows for evaluation of both global and focal myocardial function, and is based on speckle-tracking ultrasonographic assessment of parameters such as velocity and myocardial strain.

Ultrasonographic assessment of fetal myocardial function employs both M-mode imaging and color Doppler imaging. In clinical practice, strain, strain rate, and rotational mechanics are routinely used for serial assessment of fetal cardiac function. However, there are limitations related to the scanning area when evaluating whole-heart movement using these two imaging methods: M-mode imaging can only capture images along the sonar line, and color Doppler has a similar limitation due to ultrasonic refraction angles. VVI visualizes locoregional movements of speckled structures to enable whole cardiac analysis, including the quantification of velocity and strain without limitations of ultrasonic refraction angles. VVI demonstrates increasing vector velocities during normal gestation as a result of somatic growth rather than changes in myocardial contractility. Although 2D strain demonstrated any deformation on the right ventricle, a significantly higher
deformation was detectable on the normal lateral atrial wall. Global ventricular longitudinal velocity (GVLV) gradually increases throughout the gestational period and is generally higher in the right ventricle (RV) than in the left ventricle (LV), although systolic GVLV of the LV approaches that of the RV in the third trimester. Importantly, however, these findings were obtained from sporadic surveillance studies that observed fetuses at random sampling points. Only one report indicated that pre-eclampsia may impair fetal myocardial function in the RV. In the present study, we examined fetal ventricular function throughout gestation to re-evaluate the accurate significance of VVI.

Materials and methods

Participants

We prospectively examined 50 consecutive pregnant women who underwent prenatal care at Iwate Medical University Hospital during their second and third trimesters in 2016 and 2017. Of these, 29 women had growth-normal singleton fetuses, while 21 had fetuses with fetal growth restriction (FGR). Gestational age was estimated based on either crown-rump length measurements or the date of the participant’s last menstruation, according to the guidelines of the Japan Society of Obstetrics and Gynecology. Routine fetal ultrasound examinations were performed by one of seven obstetricians in the department. Fetal weight was estimated using methods recommended by the Japan Society of Ultrasonics in Medicine. All fetuses underwent echocardiography examinations roughly every two weeks, and cardiac images from these sessions were recorded. The fetuses defined as normal exhibited no FGR (estimated fetal body weight < −1.5 SD), congenital anomaly, or chromosomal abnormality, and they did not require any intervention after delivery. This study was approved by the institutional ethical committee of Iwate Medical University Hospital (H28–18). Informed consent was obtained from all participants after they were briefed on the research process and outcomes.

Image acquisition

We used an ACUSON2000 (Mochida Siemens Medical System, Japan) equipped with a CH 6–2 transducer (2–6 MHz) to obtain both apical and basal four-chamber view movies of two to three cardiac cycles recorded in 2D images, paying special attention to ensure a high frame rate (≥60 frames/s; range, 60–171 frames/s; median rate, 85 frames/s). Two examiners (N.N. and C.I.) performed all measurements in the present study. Images were stored in the Digital Imaging and Communications in Medicine (DICOM) format.

Image analysis

Offline VVI analysis was performed using the workstation Syngo VVI (Mochida Siemens Medical System) by a single interpreter (N.N.) to minimize the effect of observer measurement variability. First, heart rate was determined using M-mode cardiac images, because offline VVI cannot record fetal electrophysiologic signals. Second, the inner walls of the atria and ventricles were manually traced on captured images. The following parameters (A–C) were then automatically calculated for both ventricles based on the VVI analysis (Figure 1).

A) Global longitudinal velocity (GLV) of the left ventricle in systole (LVs), left ventricle in diastole (LVD), right ventricle in systole (RVs), and right ventricle in diastole (RVD)

B) Segmental longitudinal velocity (systolic and diastolic)

C) Global longitudinal systolic strain (GS) and strain rate (GSR)

The cardiac free wall and the septum of each ventricle were segmented into three parts: base, middle, and apex. Peak longitudinal velocity, strain, and strain rate were calculated for each segment (segmental: B). Global values were also obtained as the average of segmental parameters (global: A and C). Changes in each parameter were tracked over the gestational course (Figure 2).

D) One-time fetal cardiac functional assessment in normal and FGR cases

In both normal singleton and FGR cases with and without HDP, fetal cardiac VVI analysis was performed for GLV, GS, and GSR of LVs and RVs, and GLV of LVD and RVD. In FGR cases, analysis was performed during arbitrary prenatal care visits in the third trimester.

E) Inter-examiner measurement variability

We compared the outcomes of two independent operators (N.N. and R.O.) to test inter-examiner agreement for GLV, GS, and GSR of LVs from 10 randomly selected participants.

Figure 1. Fetal myocardial performance using the Syngo VVI.

Each arrow represents the ventricular wall velocity in (A) the left ventricle in systole (LVs) and (B) the right ventricle in systole (RVs).
Fetal myocardial evaluation with VVI

Statistical analyses
The Mann-Whitney U-test was used to compare the two groups, and regression analysis with a 95% confidence interval (CI) was performed to examine global longitudinal peak velocity throughout gestation. Inter-examiner measurement agreement was evaluated by calculating the intraclass correlation coefficient (ICC). *P* < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS for Windows version 20.0 (SPSS Japan Inc, Tokyo).

Results
Serial fetal cardiac functional assessment in normal singleton cases
We prospectively examined 170 images (an average of 6.4 images per participant) from 29 consecutive pregnant women (age range, 23–42 years; median, 34 years) who attended the prenatal care unit at Iwate Medical University during their second and third trimester (gestational age range, 15–36 weeks; median, 25 weeks). The success rate of image analysis was 74% (125/170 images). Blurred images were attributed to inaccurate tracing, maternal obesity, fetal malposition, and fetal movement. In 13 of the 29 cases, satisfactory images were captured serially more than four times, and

Figure 2. VVI vector and velocity analysis of the right ventricle (RV).
The analysis automatically divides the ventricle into six segments (free wall: base, middle, and apex; septum: base, middle, and apex).

Figure 3. Changes in global longitudinal velocity (GLV) with gestational age in 13 cases during systole (A) and diastole (B). Left ventricle (LV) values are shown in blue and green, and right ventricle (RV) values are shown in red and purple.
Figure 4. Changes in segmental longitudinal systolic velocity with gestational age in 13 cases. Left ventricle (LV) values are shown in blue and green, and right ventricle (RV) values are shown in red and purple. Free wall basal and middle longitudinal systolic velocities of the LV and RV and septum basal and middle longitudinal systolic velocities of the LV are shown.

Figure 5. Changes in segmental longitudinal diastolic velocity with gestational age in 13 cases. Left ventricle (LV) values are shown in blue and green, and right ventricle (RV) values are shown in red and purple. Free wall basal and middle longitudinal diastolic velocities of the LV and RV, free wall and septum apical longitudinal diastolic velocities of the LV and RV, and septum basal and middle longitudinal diastolic velocities of the LV are shown.
statistical analyses were carried out on data from each of these 13 normal cases (82 images).

**A) Global longitudinal velocity in normal singleton cases**

GLV of LVs and RVs significantly increased with gestational age in 13 fetuses (100%; \( P < 0.05 \)) and 11 fetuses (84.6%; \( P < 0.05 \)), respectively. GLV of LVd and RVd significantly increased with gestational age in 10 fetuses (76.9%; \( P < 0.05 \)) (Figure 3).

**B) Segmental longitudinal velocity in normal singleton cases**

The basal and middle longitudinal velocities of the free wall in both the LV and RV significantly increased in 10 fetuses during systole (76.9%; \( P < 0.05 \)) and in eight fetuses during diastole (61.5%; \( P < 0.05 \)). No gestational age-related changes were observed in the longitudinal velocity of the apical free wall in either the LV or RV during systole or diastole (23.1%–46.2%; \( P < 0.05 \)). In the septum, the basal and middle longitudinal velocities tended to increase with gestational age (53.8%–69.2%; \( P < 0.05 \)). In the apical segment of the LV septum and all three segments of the RV septum (basal, middle, and apical), systolic velocity showed no significant changes with gestational age (15.4%–46.2%; \( P < 0.05 \)) (Figure 4 and Figure 5, Table 1).

**C) Global longitudinal systolic strain and strain rate in normal singleton cases**

The GS and GSR of both ventricles showed no differences according to gestational age (0%–30%; \( P < 0.05 \)) (Figure 6).

**D) One-time fetal cardiac functional assessment in normal and FGR cases**

There was no significant difference between normal singleton (\( n = 27 \)) and FGR (\( n = 21 \)) cases in terms of gestational week during which participants were examined (31.50 ± 2.24 vs. 32.60 ± 3.64; \( P = 0.90 \)). GLV of LVs was significantly lower in fetuses with FGR compared to normal fetuses (\( P = 0.029 \)). RVs and RVd tended to show lower FGR, but there were no significant differences (\( P = 0.090 \)). There were also no significant differences in GS, GSR, or GLV of LVs and RVd (Table 2). Eight of the 21 FGR fetuses with HDP appeared to have low LVd and RVs, but there were no significant differences compared to the other 13 without HDP (\( P = 0.090 \). Table 2 and Table 3).

**E) Inter-examiner agreement in the VVI analysis of normal singleton cases**

To assess the reproducibility of VVI analysis, the ICC between the two examiners was calculated for 10

---

### Table 1. Regression analysis of global longitudinal velocity (GLV) for 13 cases, with gestational period as a factor

<table>
<thead>
<tr>
<th>Case Number</th>
<th>Number of images</th>
<th>LVs (cm/s)</th>
<th>RVs (cm/s)</th>
<th>LVd (cm/s)</th>
<th>RVd (cm/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>y = 0.44 ± 0.06x</td>
<td>0.971</td>
<td>0.000</td>
<td>y = 0.59 ± 0.071x</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>y = 0.29 ± 0.05x</td>
<td>0.932</td>
<td>0.000</td>
<td>y = 0.96 ± 0.092x</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>y = 1.06 ± 0.10x</td>
<td>0.984</td>
<td>0.000</td>
<td>y = 0.24 ± 0.061x</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>y = 1.05 ± 0.10x</td>
<td>0.989</td>
<td>0.005</td>
<td>y = 0.33 ± 0.094x</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>y = 0.73 ± 0.05x</td>
<td>0.983</td>
<td>0.018</td>
<td>y = 0.50 ± 0.061x</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td>y = 0.73 ± 0.05x</td>
<td>0.985</td>
<td>0.018</td>
<td>y = 0.66 ± 0.081x</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
<td>y = 0.71 ± 0.05x</td>
<td>0.987</td>
<td>0.013</td>
<td>y = 0.33 ± 0.085x</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>y = 0.71 ± 0.05x</td>
<td>0.985</td>
<td>0.018</td>
<td>y = 0.50 ± 0.061x</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
<td>y = 0.52 ± 0.05x</td>
<td>0.987</td>
<td>0.013</td>
<td>y = 0.33 ± 0.085x</td>
</tr>
<tr>
<td>10</td>
<td>11</td>
<td>y = 1.24 ± 0.10x</td>
<td>0.976</td>
<td>0.004</td>
<td>y = 0.22 ± 0.061x</td>
</tr>
<tr>
<td>11</td>
<td>6</td>
<td>y = 0.52 ± 0.05x</td>
<td>0.987</td>
<td>0.013</td>
<td>y = 0.50 ± 0.061x</td>
</tr>
<tr>
<td>12</td>
<td>5</td>
<td>y = 0.71 ± 0.05x</td>
<td>0.987</td>
<td>0.013</td>
<td>y = 0.33 ± 0.085x</td>
</tr>
<tr>
<td>13</td>
<td>8</td>
<td>y = 0.73 ± 0.05x</td>
<td>0.985</td>
<td>0.018</td>
<td>y = 0.50 ± 0.061x</td>
</tr>
</tbody>
</table>

LVs, left ventricle in systole; LVd, left ventricle in diastole; RVs, right ventricle in systole; RVd, right ventricle in diastole. Gray zones: \( P > 0.05 \). Equation: regression expression (y, velocity; x, gestational age), \( R^2 \): coefficient of determination.
Table 2. Comparison between cases of fetal growth restriction (FGR) with and without hypertensive disorders of pregnancy (HDP)

<table>
<thead>
<tr>
<th></th>
<th>FGR (n = 21)</th>
<th>HDP (n = 8)</th>
<th>no HDP (n = 13)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>34.89 ± 4.08</td>
<td>30.62 ± 5.32</td>
<td>0.066</td>
<td></td>
</tr>
<tr>
<td>Gestational week at examination</td>
<td>31.38 ± 3.02</td>
<td>33.31 ± 3.84</td>
<td>0.118</td>
<td></td>
</tr>
<tr>
<td>Gestational week on delivery</td>
<td>32.89 ± 4.46</td>
<td>37.46 ± 2.90</td>
<td>0.021</td>
<td></td>
</tr>
<tr>
<td>Newborn weight (g)</td>
<td>1,222.78 ± 542.46</td>
<td>2,089.58 ± 442.37</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>GLV of LVs (cm/s)</td>
<td>1.186 ± 0.321</td>
<td>1.355 ± 0.447</td>
<td>0.426</td>
<td></td>
</tr>
<tr>
<td>GLV of LVd (cm/s)</td>
<td>−1.330 ± 0.283</td>
<td>−1.785 ± 0.616</td>
<td>0.090</td>
<td></td>
</tr>
<tr>
<td>GS of LVs (%)</td>
<td>−16.597 ± 5.233</td>
<td>−18.330 ± 5.233</td>
<td>0.385</td>
<td></td>
</tr>
<tr>
<td>GSR of LVs (%/s)</td>
<td>−1.93 ± 0.514</td>
<td>−2.085 ± 0.620</td>
<td>0.664</td>
<td></td>
</tr>
<tr>
<td>GLV of RVs (cm/s)</td>
<td>1.322 ± 0.242</td>
<td>1.616 ± 0.435</td>
<td>0.096</td>
<td></td>
</tr>
<tr>
<td>GLV of RVd (cm/s)</td>
<td>−1.796 ± 0.440</td>
<td>−2.014 ± 0.583</td>
<td>0.311</td>
<td></td>
</tr>
<tr>
<td>GS of RVs (%)</td>
<td>−17.466 ± 1.982</td>
<td>−19.649 ± 4.038</td>
<td>0.277</td>
<td></td>
</tr>
<tr>
<td>GSR of RVs (%/s)</td>
<td>−1.996 ± 0.323</td>
<td>−2.206 ± 0.492</td>
<td>0.311</td>
<td></td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. All P-values were calculated using the Mann-Whitney test. GLV, global longitudinal velocity; GS, global strain; GSR, global strain rate; LVs, left ventricle in systole; LVd, left ventricle in diastole; RVs, right ventricle in systole; RVd, right ventricle in diastole.

Figure 6. Changes in global longitudinal systolic strain (A) and strain rate (B) with gestational age in 13 cases. Longitudinal strain and strain rate values are negative in systole. Left ventricle (LV) values are shown in blue and green, and right ventricle (RV) values are shown in red and purple. Global longitudinal systolic strain of the LV and RV, and global longitudinal systolic strain rate of the LV and RV are shown.

randomly selected normal cases. The mean GLV of LVs was 0.855 (95% CI: 0.520–0.962), mean GS of LVs was 0.73 (95% CI: 0.228–0.925), and mean GSR of LVs was 0.492 (95% CI: 0.157–0.884).

Discussion

VVI is suitable for evaluating cardiac function. However, no comprehensive studies in fetuses have been conducted due to several technical obstacles in capturing satisfactory images such as unexpected fetal movement, image-resolution changes corresponding to fetal cardiac enlargement, and manual tracing on the small cardiac walls during early gestational stages. Several studies have assessed myocardial development in randomly assigned fetuses, but 26% of single-time VVI analyses were unsatisfactory in these studies, indicating the unreliability of such analyses. In the present study, one examiner (N.N.) examined VVI, carrying out four or more serial VVI tracking analyses in each pregnant woman during the second and third trimester. This is the first longitudinal study to address ventricular function in individual fetuses according to gestational age.
The results of the present study show that, over the second and third trimester, GLV increases in LVs, RVs, LVd, and RVd. Previous studies based on randomly assigned samples have also reported increases in GLV of normal singleton fetuses throughout the second and third trimester of gestation. However, to date, no studies have clarified how fetal cardiac movement in normal singletons changes throughout gestation. Rudolph and Heymann showed that, in the fetal lamb, the combined ventricular output (CVO: the standard for expressing fetal heart output) is constant from 40 to 140 days of gestation (term), at 450–500 ml/min/kg fetal weight. In human fetuses, it has also been established that CVO is constant at about 450 ml/min/kg fetal weight over the latter two-thirds of gestation, and that cardiac chamber development is influenced by blood flow. The GLV increases observed in the present study might be attributed to the increase in the systemic circulation volume of the fetal body.

**Segmental longitudinal velocity**

In the present study, the increases in velocity of the LV corresponded with gestational age. Moreover, the increases in GLV of the LV were especially marked at the basal and middle portions of the free wall. As the inner muscular bundle of the ventricles runs longitudinally, VVI procedures that trace ventricular walls is anatomically suitable for evaluating LV myocardial development.

**Global longitudinal systolic strain and strain rate**

The GS and GSR of both ventricles showed no differences according to gestational age, approaching the expected values for gestational age over time. This might be because the GS and GSR values were appropriate for about 25 weeks of gestation. Figure 6 shows 25 weeks varied negligible. Preterm infants reportedly show stable longitudinal strain on both sides of the ventricular septum, RV free wall, and the LV, despite hemodynamically significant changes during the first 72 hs of life. Therefore, the results of the present study suggest that GS and GSR, which represent myocardial contraction activity, remain relatively stable throughout gestation, and that they may serve as indicators of myocardial deployment that increase with increasing fetal weight.

**One-time fetal cardiac functional assessment in normal and FGR cases**

In the present study, GLV of LVs was lower in FGR cases compared to normal cases, which corroborates previous studies carried out without serial VVI assessment. Furthermore, no remarkable differences were observed in GLV of LVs between FGR cases with HDP and those without HDP (Table 2). The ensuing mismatch between fetal demands and utero-placental supply results in systemic maternal and fetal inflammatory manifestations, which then trigger fetal compensatory mechanisms that cause fetal cardiac compromise and inadequate tissue perfusion. In the present study, LV and RV function in FGR cases with HDP appeared to be suppressed; the low value was not significant but non-negligible in the GLV of LVd and RVs, which could result in the absence of blood flow.

**Inter-examiner agreement in VVI analysis**

This study has two important limitations. First, the sample size was small. Second, there may be a lack of...
reproducibility in evaluating fetal cardiac function with VVI in real time at a correct position using a manual method. However, the evaluation of inter-examiner reproducibility showed a high concordance, especially for GLV of LVs (0.855), GS of LVs (0.73), and GSR of LVs (0.49), indicating the universal validity of VVI analysis.

In conclusion, the evaluation of fetal ventricular function using VVI revealed that GLV increases throughout gestation, and that values of GLV of the LV and RV tend to be lower in FGR cases with HDP compared to those without HDP.

Acknowledgments

This work was supported by JSPS Grants-in-Aid for Scientific Research (KAKENHI) (Grant No. 16K11102).

Conflict of Interest

All authors declare no conflicts of interest.

References
