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Longitudinal assessment of fetal myocardial performance index in normal pregnancy using spectral tissue Doppler

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KEYWORDS: fetal; myocardial performance index; reference range; tissue Doppler; ultrasound

ABSTRACT

Objective *Although spectral tissue Doppler imaging is recognized as the optimal method for assessing the fetal myocardial performance index (MPI), longitudinal reference ranges for fetal MPI measured using spectral tissue Doppler have not been established. Our objective was to use spectral tissue Doppler data to establish gestational-age-specific reference ranges from 12–33 weeks for left and right ventricular fetal MPI.*

Methods *This was a prospective longitudinal study of women aged 18–35 years, with a body mass index below 30 kg/m^2 and a singleton pregnancy conceived spontaneously. Fetal MPI measurements were obtained in the first, second and third trimesters and MPI was determined using spectral tissue Doppler imaging. A generalized additive model for location, scale and shape (GAMLSS) was used to explore the relationship between fetal MPI and gestational age. Model fit was assessed by checking the normality of estimated Z-scores across the fitted range and independency from gestational age.*

Results *Median fetal MPI was determined for the right and left ventricles at 12–13 weeks, 20–21 weeks and 32–33 weeks' gestation in 90 fetuses. Using multilevel regression modeling, weekly reference ranges for each gestational age were created to provide a continuous characterization of normal fetal MPI assessed using spectral tissue Doppler throughout pregnancy. Percentile reference ranges (5th, 10th, 25th, 50th, 75th, 90th and 95th) for right and left ventricular fetal MPI were generated from these models, capturing normal variability across gestation.*

Conclusion *We have established gestational-age-specific reference ranges for left and right ventricular fetal MPI using spectral tissue Doppler imaging, thus providing clinicians with an important tool for the early detection of fetal cardiac dysfunction in high-risk pregnancies.* © *2025 The Author(s). Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of International Society of Ultrasound in Obstetrics and Gynecology.*

INTRODUCTION

Assessment of fetal cardiac function is increasingly recognized as an important step in fetal evaluation, particularly in the presence of uteroplacental insufficiency[1,2]. Evaluation of fetal cardiac function reflects placental vascular function and perfusion from the fetal side, and can differentiate between compensated and non-compensated responses to placental insufficiency[2,3]. If uteroplacental insufficiency is present, changes in fetal cardiac function occur before changes in Doppler findings of the fetal peripheral vessels, which reflect late adaptation to disease states[2,3].

The myocardial performance index (MPI) is one of the measures used to assess fetal cardiac function. MPI, also known as the Tei index, is a Doppler-derived, non-invasive method of assessing global cardiac systolic and diastolic function[4,5]. The MPI is calculated by adding the isovolumetric contraction time and isovolumetric relaxation time, then dividing by the ejection time (ET). This requires measurement of the time interval between the end and onset of mitral or tricuspid inflow, as well as the ET of the left (LV) or right ventricle (RV) outflow.

Multiple techniques have been employed to assess fetal MPI. Spectral tissue Doppler measures the velocity of myocardial tissue directly, whereas pulsed-wave Doppler evaluates blood flow through the cardiac

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valves[6]. Recently, spectral tissue Doppler has emerged as superior to pulsed-wave Doppler for assessing fetal MPI because it directly measures myocardial motion with higher temporal resolution, reduced angle dependence and greater sensitivity to changes in cardiac function[7–12]. These advantages allow more precise, reproducible and reliable MPI measurements, especially for the early detection of fetal cardiac dysfunction[7–12].

Previous studies have proposed reference ranges for fetal MPI using pulsed-wave Doppler[12–16]. Fetal MPI measurements obtained using pulsed-wave Doppler and spectral tissue Doppler differ significantly, likely owing to their different postprocessing and temporal resolution techniques, and cannot be used interchangeably[17–19]. Although spectral tissue Doppler imaging is recognized as the optimal method for assessing fetal MPI[20], reference ranges throughout pregnancy for fetal MPI measured using spectral tissue Doppler have not been established.

Our objective was to use spectral tissue Doppler data to establish gestational-age-specific reference ranges for fetal MPI of the RV and LV.

METHODS

This was a prospective longitudinal study that utilized data from the Human Placenta Project cohort (study: HD 086313-01), funded by the National Institutes of Health. Patients were recruited from the Eastern Virginia Medical School (EVMS) prenatal care clinic in Norfolk, VA, USA, and the University of Texas Medical Branch (UTMB) in Galveston, TX, USA, between January 2016 and March 2020. Written informed consent was obtained from all participants prior to enrolment, and the study protocol was approved by the EVMS and UTMB Institutional Review Boards (IRB:15-09-FB-0179). Both ultrasound units are accredited by the American Institute of Ultrasound in Medicine and adhere to the as low as reasonably achievable (ALARA) principle for ultrasound safety. Eligible participants were women aged 18–35 years, with a body mass index below 30 kg/m^2 and a singleton pregnancy conceived spontaneously. Enrolment occurred at or before 13 + 6 weeks' gestation. Participants of the Human Placenta Project underwent a series of eight longitudinal ultrasound examinations, commencing at 12 + 0 to 13 + 6 weeks and continuing until 36 + 0 to 37 + 6 weeks. Baseline characteristics and outcome data were recorded by trained research coordinators. Spectral tissue Doppler measurements were obtained only at the EVMS site.

For this analysis, only data from pregnancies delivered ≥ 37 weeks with uncomplicated maternal and neonatal outcomes were included. Pregnancies with a maternal or neonatal complication, fetal or umbilical cord anomaly at the time of recruitment in the first trimester, abnormal placental implantation or delivery before 37 weeks were excluded. Abnormal placental implantation was defined as placenta previa (placenta covering the internal cervical os) or bilobed placenta, identified during first-trimester recruitment. Umbilical cord abnormality was defined as marginal or velamentous cord insertion, identified during first-trimester recruitment. The final reference population comprised participants who met all the eligibility criteria, ensuring a cohort of uncomplicated pregnancies with normal outcomes.

Fetal MPI measurements were obtained at the first (12–13 weeks), fourth (20–21 weeks) and seventh (32–33 weeks) ultrasound visits. All examinations were performed transabdominally using Toshiba Aplio™ i500 or Canon Aplio™ i800 ultrasound systems equipped with i8Cx1 convex transducers (Canon Medical Corp., Tochigi, Japan). Sonographers performing the measurements are certified in fetal echocardiography and had completed a quality assurance review of five ultrasound examinations prior to participation in the study. Measurements were independently reviewed by two remote examiners for quality assurance.

Fetal MPI was determined using spectral tissue Doppler imaging. An apical or basal 4-chamber view was obtained, and spectral tissue Doppler mode was activated with the ultrasound beam maintained at an angle of < 30° to the interventricular septum. The sample volume was placed on the lateral aspect of the tricuspid valve for the RV, and the lateral aspect of the mitral valve for the LV, to capture peak annular velocities, generating waveforms for analysis. The waveform for each ventricle was then used to obtain the isovolumetric relaxation time, ET and isovolumetric contraction time to calculate right and left ventricular fetal MPI (Figure 1).

Statistical analysis

MPI data are presented as median (interquartile range (IQR)). A generalized additive model for location, scale and shape (GAMLSS) was used to explore the relationship between fetal MPI and gestational age. Restricted cubic splines were employed where necessary to account for non-linearity. Missing values for MPI were handled using multivariate imputation by chained equations. Candidate models were compared using the likelihood ratio test. Multiple measurements from the same patient were accounted for by using random intercepts for patients and slopes for gestational age. Model fit was assessed as described by Royston and Wright[21] by checking the normality of estimated Z-scores across the fitted range and independency from gestational age. All statistical analysis was performed using R for Statistical Computing, version 4.2.0 (https://www.r-project.org/; R Foundation for Statistical Computing, Vienna, Austria). $P < 0.05$ was considered to indicate statistical significance.

RESULTS

Overall, a total of 610 women were enrolled in the Human Placenta Project between January 2016 and March 2020. 90 women fulfilled the eligibility criteria and were included in this analysis. Maternal demographics are presented in Table 1. At 12–13 weeks, the median fetal MPI for the RV was 0.46 (IQR, 0.38–0.56), increasing to

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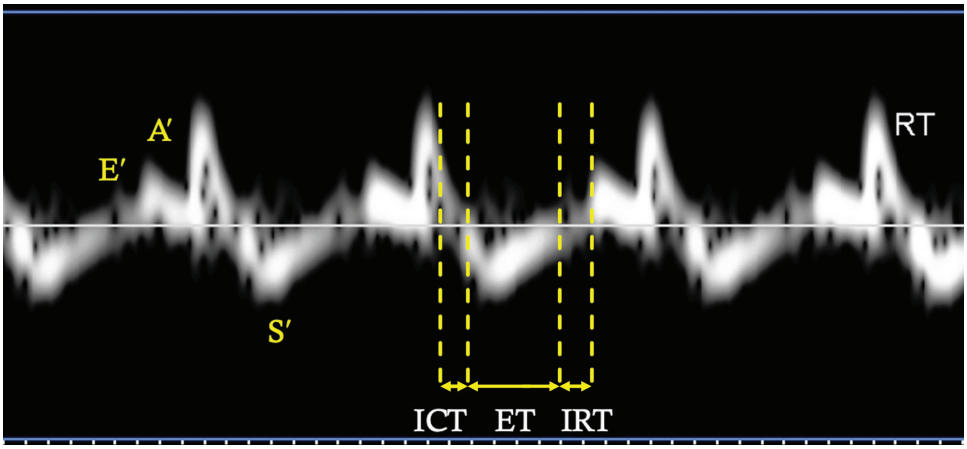


Figure 1 Representative spectral tissue Doppler waveform used to calculate fetal myocardial performance index. A′, late diastolic (atrial contraction) myocardial velocity; E′, early diastolic myocardial velocity; ET, ejection time; ICT, isovolumetric contraction time; IRT, isovolumetric relaxation time; RT, right ventricle; S′, peak systolic myocardial velocity.

Table 1 Maternal demographic characteristics and placental location in 90 patients with normal singleton pregnancy included in study

Characteristic	*Value*
Age (years)	25.52 ± 4.08
Height (cm)	163.29 ± 7.95
Weight (kg)	63.73 ± 10.36
Body mass index (kg/m^2)	23.62 ± 3.20
Race	
White	39 (43.3)
Black/African American	50 (55.6)
Asian	0 (0)
American Indian or Native American	0 (0)
Native Hawaiian or other Pacific Islander	0 (0)
Other	1 (1.1)
Ethnicity	
Hispanic/Latina	7 (7.8)
Non-Hispanic/Latina	83 (92.2)
Placental location	
Anterior	45 (50.0)
Posterior	38 (42.2)
Right lateral	1 (1.1)
Left lateral	1 (1.1)
Not reported	5 (5.6)

Data are given as mean ± SD or *n* (%).

0.55 (IQR, 0.48–0.65) at 20–21 weeks and 0.62 (IQR, 0.55–0.72) at 32–33 weeks. For the LV, the median fetal MPI was 0.51 (IQR, 0.42–0.60) at 12–13 weeks, increasing to 0.56 (IQR, 0.48–0.65) at 20–21 weeks and 0.59 (IQR, 0.50–0.68) at 32–33 weeks.

Using multilevel regression modeling, weekly reference ranges were created for each gestational age to provide a continuous characterization of normal fetal MPI assessed using spectral tissue Doppler throughout pregnancy. Percentile reference ranges (5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles) for right and left ventricular fetal MPI were generated from these models, capturing normal variability across gestation. Figure 2 illustrates the modeled percentile trajectories as gestational age increases. The percentile reference ranges by week of gestation derived from these models are presented in Table 2.

DISCUSSION

In this study, we have established gestational-age-specific reference ranges for fetal MPI of both the RV and the LV using spectral tissue Doppler, leveraging a longitudinal dataset from a rigorously defined population of normal singleton pregnancies.

This study highlights the fact that fetal MPI assessed using spectral tissue Doppler increases progressively throughout gestation for both ventricles in normal pregnancy. This is in contrast to a previous cross-sectional study of Willruth *et al.*[19] that attempted to establish normal values for fetal MPI in the second and third trimesters using spectral tissue Doppler, and noted no difference in MPI based on gestational age. Similarly, in their cross-sectional study, Comas *et al.*[22] found no change in fetal MPI of the RV using spectral tissue Doppler during the second and third trimesters of pregnancy, but did note an increase in fetal MPI of the LV. The difference in our findings is likely owing to the prospective longitudinal design of our study and our strict definition of normal pregnancy. The studies of Comas *et al.*[22] and Wilruth *et al.*[19] were both cross-sectional in design, limiting their ability to capture individual fetal cardiac adaptation over time. In contrast, this study provides longitudinal spectral tissue Doppler measurements of fetal MPI from the first trimester through to the third trimester. By applying advanced modeling techniques, we derived gestational-age-specific reference ranges for each ventricle, allowing for a more precise understanding of normal fetal cardiac function throughout pregnancy. This longitudinal approach provides critical insights into the trajectory of fetal myocardial performance, which cannot be inferred from cross-sectional studies.

Our data also demonstrate that normal fetal MPI values of the RV and LV assessed using spectral tissue Doppler differ throughout pregnancy. The fetal RV plays a dominant role in fetal circulation, contributing approximately 60% of cardiac output. Therefore, the RV is particularly sensitive to hemodynamic disturbances

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that arise in conditions such as fetal growth restriction (FGR) and placental insufficiency[11]. In the presence of FGR, fetal MPI is affected early in the course of hypoxemia and remains abnormal during various phases of fetal compromise[23]. MPI is prolonged in FGR fetuses, even in the presence of forward flow in the umbilical artery, confirming that it is an early marker of fetal compromise[24]. This understanding of the critical role of the RV in fetal circulation and its sensitivity to hemodynamic disturbances underscores the importance of establishing accurate reference ranges for MPI, particularly in assessing fetal wellbeing across different

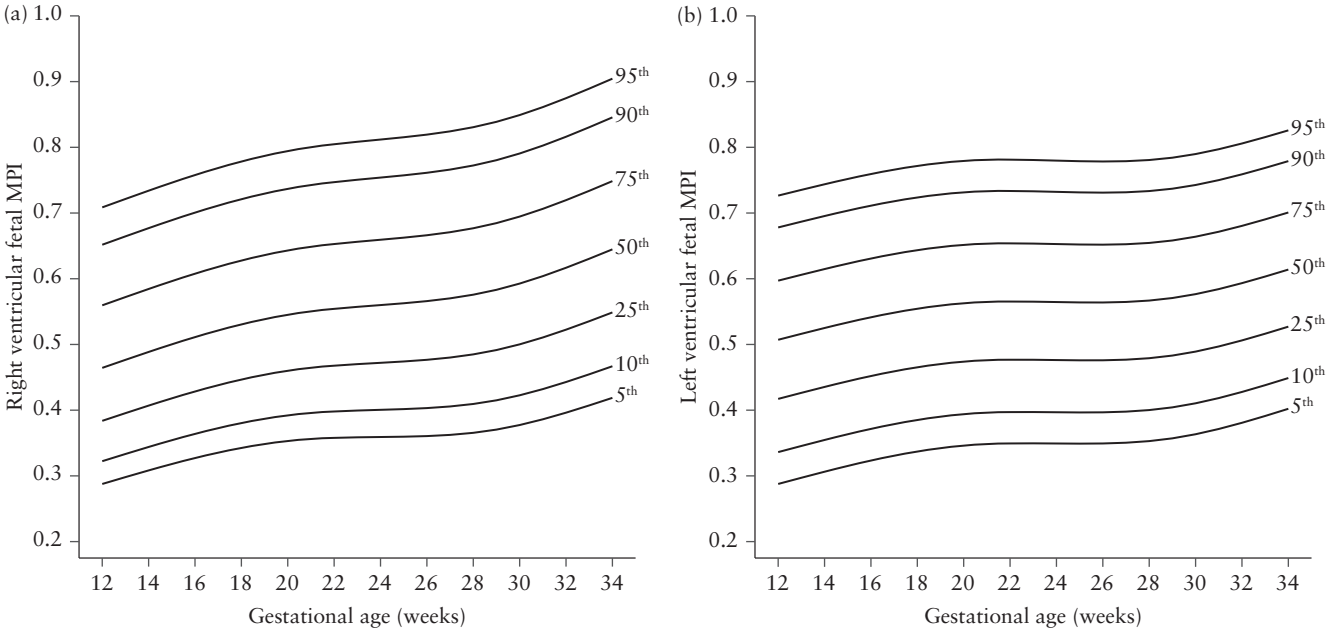


Figure 2 Scatterplots showing reference ranges for fetal myocardial performance index (MPI), measured using spectral tissue Doppler, of right (a) and left (b) ventricles, according to gestational age, in uncomplicated singleton pregnancies. The 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles are shown.

Table 2 Right and left ventricular fetal myocardial performance index (MPI) reference ranges, measured using spectral tissue Doppler, according to gestational age (GA), from 12–34 weeks' gestation in uncomplicated singleton pregnancies

	Percentile													
	Right ventricular fetal MPI							*Left ventricular fetal MPI*						
GA (weeks)	*5th*	*10th*	*25th*	*50th*	*75th*	*90th*	*95th*	*5th*	*10th*	*25th*	*50th*	*75th*	*90th*	*95th*
12	0.288	0.322	0.384	0.464	0.560	0.652	0.709	0.288	0.336	0.417	0.507	0.597	0.678	0.727
13	0.298	0.333	0.395	0.477	0.572	0.664	0.721	0.297	0.346	0.426	0.516	0.606	0.687	0.735
14	0.308	0.344	0.407	0.489	0.584	0.677	0.734	0.306	0.355	0.435	0.525	0.615	0.695	0.744
15	0.318	0.354	0.418	0.500	0.596	0.689	0.746	0.315	0.363	0.444	0.533	0.623	0.704	0.752
16	0.327	0.364	0.428	0.511	0.608	0.701	0.758	0.323	0.371	0.452	0.541	0.631	0.711	0.759
17	0.335	0.373	0.438	0.521	0.618	0.711	0.769	0.331	0.379	0.459	0.548	0.638	0.718	0.766
18	0.343	0.380	0.447	0.531	0.628	0.721	0.778	0.337	0.385	0.465	0.554	0.644	0.724	0.772
19	0.349	0.387	0.454	0.539	0.636	0.730	0.787	0.342	0.390	0.470	0.559	0.648	0.728	0.776
20	0.353	0.392	0.460	0.545	0.643	0.737	0.794	0.346	0.394	0.474	0.563	0.652	0.731	0.779
21	0.356	0.396	0.464	0.550	0.649	0.743	0.800	0.348	0.396	0.476	0.565	0.653	0.733	0.781
22	0.358	0.398	0.468	0.554	0.653	0.747	0.805	0.349	0.397	0.477	0.565	0.654	0.734	0.781
23	0.359	0.399	0.470	0.557	0.656	0.751	0.808	0.350	0.397	0.477	0.565	0.654	0.733	0.781
24	0.359	0.401	0.472	0.560	0.659	0.754	0.812	0.349	0.397	0.476	0.565	0.653	0.732	0.780
25	0.360	0.402	0.474	0.563	0.663	0.757	0.815	0.349	0.397	0.476	0.564	0.652	0.731	0.779
26	0.361	0.403	0.477	0.566	0.666	0.761	0.819	0.349	0.397	0.476	0.564	0.652	0.731	0.778
27	0.362	0.406	0.480	0.570	0.671	0.766	0.824	0.350	0.398	0.477	0.565	0.653	0.732	0.779
28	0.366	0.409	0.485	0.576	0.677	0.772	0.831	0.353	0.400	0.479	0.567	0.654	0.733	0.781
29	0.370	0.415	0.491	0.583	0.685	0.780	0.839	0.357	0.404	0.483	0.571	0.658	0.737	0.784
30	0.377	0.423	0.500	0.593	0.695	0.791	0.849	0.363	0.410	0.489	0.577	0.664	0.743	0.790
31	0.386	0.432	0.511	0.604	0.706	0.803	0.861	0.371	0.418	0.497	0.584	0.672	0.750	0.797
32	0.396	0.443	0.523	0.617	0.720	0.816	0.875	0.381	0.428	0.506	0.593	0.680	0.759	0.806
33	0.407	0.455	0.535	0.630	0.734	0.831	0.889	0.391	0.438	0.516	0.603	0.690	0.769	0.816
34	0.419	0.467	0.549	0.645	0.749	0.846	0.904	0.402	0.449	0.527	0.614	0.701	0.779	0.826

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pathological states. We believe the RV is most suited for MPI evaluation in the fetus, as fetal MPI measurements of the the RV have been shown to detect early cardiac dysfunction, even when other indicators remain normal[16].

The establishment of gestational-age-specific reference ranges for fetal MPI using spectral tissue Doppler advances the assessment of fetal cardiac function *in-utero*. This study addresses the need for reference ranges in early pregnancy, which is a critical step in further assessing the clinical utility of fetal MPI using spectral tissue Doppler throughout gestation in complicated pregnancies. Future studies should focus on assessing if abnormal fetal MPI values can serve as early indicators for the need for increased surveillance and potential intervention in pregnancies at risk of fetal compromise.

This study has several strengths. The longitudinal design allowed for a comprehensive assessment of fetal cardiac function throughout pregnancy. The statistical analysis was thorough, with multiple checks for outliers, normality of residuals and autocorrelation. By allowing model intercepts to vary between individuals, differences in fetal development were accounted for while still generating normative curves that are generalizable to the population.

Despite the strengths of this study, some limitations should be considered. First, the study included only women with an uncomplicated pregnancy and a body mass index below 30 kg/m^2, which may limit the generalizability of the findings to a broader population, particularly women with obesity or other comorbidities. Additionally, although spectral tissue Doppler is a valuable tool for measuring MPI, it requires specialized equipment and operator training, which may limit its widespread use in clinical practice.

In conclusion, we have established gestational-age-specific reference ranges for left and right ventricular fetal MPI using spectral tissue Doppler imaging. These reference ranges can provide clinicians with an important tool for the early detection of fetal cardiac dysfunction in high-risk pregnancies. Future research should focus on expanding the applicability of these reference ranges to a more diverse population and on further validating their use in predicting adverse perinatal outcomes.

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