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Gestational-age-adjusted reference values for the modified myocardial performance index for evaluation of fetal left cardiac function

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KEYWORDS: Doppler; fetal cardiac function; modified myocardial performance index

ABSTRACT

Objective *It has been shown that the modified myocardial performance index (Mod-MPI) is associated with higher reproducibility than conventional MPI because it uses mitral and aortic valve 'clicks' to calculate each time period. We aimed to construct normal reference values for the Mod-MPI after 19 weeks' gestation.*

Methods *The Mod-MPI was calculated in the left ventricle of 557 normal fetuses at 19–39 weeks' gestation. The isovolumetric contraction time (ICT), isovolumetric relaxation time (IRT) and ejection time (ET) were measured using the Doppler signals (clicks) of the opening and closing of the mitral and aortic valves as landmarks. Mod-MPI was calculated as (ICT + IRT)/ET.*

Results *Throughout gestation, there was a small increase in the Mod-MPI (at 19 weeks it was 0.35 ± 0.027 (mean ± SD); at 39 weeks, 0.37 ± 0.029; Mod-MPI = $0.33 + 0.001 \times$ gestational age (GA) (weeks), $r^2 = 0.017$). Of the three components, ICT remained constant, IRT increased (IRT = $0.028 + 2.52 \times$ GA (weeks)), and ET slightly decreased (ET = $0.184 - 3.65 \times$ GA (weeks)). Fetal heart rate (FHR) had no effect on the Mod-MPI, but the duration of IRT, ICT and ET decreased by 13–15% when FHR increased from 130 to 160 beats per minute.*

Conclusion *The GA-adjusted reference values for the Mod-MPI and the three time periods used for its calculation can be applied to fetal cardiac evaluation in the presence of pregnancy-associated complications.*

INTRODUCTION

Numerous fetal and pregnancy-associated conditions have a considerable impact on the fetal heart. Consequently, evaluation of cardiac function has been increasingly performed in order to assist in clinical decision-making[1,2]. To this end, the use of different fetal cardiac parameters has been proposed, such as shortening and ejection fractions, tricuspid regurgitation, and abnormal flow in the aortic isthmus[3–5]. However, in clinical practice, most of the cardiac indices proposed are of limited applicability owing to low interobserver reproducibility.

The myocardial performance index (MPI) was first proposed by Tei *et al.*[6] for the evaluation of heart function in adults with amyloidosis. The MPI is the ratio between the duration of the isovolumetric period (composed of two periods – contraction and relaxation) and the duration of the ejection period in the cardiac ventricle. Abnormal cardiac function is associated with a prolongation of the isovolumetric period and a reduction in ejection time, thus resulting in an increase in the MPI. For the original calculation, Tei *et al.*[7] proposed the acquisition of two waveforms in different locations: first, below the atrioventricular valve to record the E/A waveform for calculation of the isovolumetric periods, and second, in the outflow tracks for the ejection period.

Although the MPI has become part of routine clinical assessment in newborns[8], in fetuses it is still under evaluation. Several authors have calculated the MPI in fetuses using the originally described technique, but the results show wide variability in the values reported for normal fetuses[9,10]. To improve the performance of this technique, Friedman *et al.*[11] suggested that the

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MPI in the left ventricle could be evaluated during the same Doppler waveform. This approach is feasible because the aorta emerges very close to the mitral valve; furthermore, it allows direct and individual measurement of isovolumetric contraction time (ICT) and isovolumetric relaxation time (IRT). However, this approach does not solve an important drawback for calculation of the MPI – i.e. the absence of clear landmarks delineating the three periods used for this calculation. A substantial improvement was achieved by Raboisson *et al.*[12], who first used the Doppler echo ('click') of the opening of the aortic valve (AV) as a landmark to better estimate the limits of the ejection period. As a further development of this idea, we recently proposed a modified MPI (Mod-MPI) in the left ventricle, which uses the opening and closing clicks of the mitral valve (MV) and AV to clearly define the three time periods used for the MPI[13]. This Mod-MPI significantly improved interobserver reproducibility as compared with the standard MPI calculation.

The aim of the present study was to construct gestational age (GA)-adjusted reference values for the Mod-MPI and for the three time periods used for its calculation according to the above-mentioned measurement technique.

METHODS

A cross-sectional study was performed in 557 normal fetuses at 19–39 weeks' gestation. The Mod-MPI was calculated in the fetal left ventricle. The median maternal age at enrolment was 26 (range, 18–32) years. Measurements obtained from women developing any complication during pregnancy or at birth were excluded from the final calculation. The project was approved by the ethics committees of both participating institutions, and written consent was obtained in all cases.

For the ultrasound and Doppler studies, a Siemens Sonoline Antares (Siemens Medical Systems, Malvern, PA, USA), a Voluson 730 Expert (GE Medical Systems, WI, USA) and a Toshiba Aplio XG (Nasu, Japan) ultrasound machine, equipped with 6–4-MHz curved probes, were used. All estimations were performed in the absence of fetal body and respiratory movements and with the mother in voluntary suspended respiration. The mechanical and thermal indices never exceeded 1.

A cross-sectional image of the fetal thorax at the level of the four-chamber view with an apical projection of the heart was obtained. By sweeping the ultrasound probe slightly in the apical direction, the origin of the aorta could be observed. The Doppler sample volume was opened to 3 mm and placed in the internal leaflet of the MV. In this location, owing to its closeness to the AV, the opening and closing AV clicks could be registered. The angle of insonation was maintained as close as possible to 0° and was always less than 30°. To clearly identify the components of the Mod-MPI, the fastest velocity (15 cm/s) of the Doppler sweep was used, and the E/A waveform was always displayed as positive flow. The Doppler gain was lowered as far as possible to clearly visualize the echoes corresponding to the opening and closing clicks of the two valves at the beginning and at the end of the E/A (mitral valve) and aortic (AV) waveforms. A high-pass wall filter was used to avoid slow blood movements. The time cursor was placed at the beginning of each Doppler click. The three time periods were estimated as follows: (1) ICT from the beginning of MV closure to AV opening; (2) ET from AV opening to closure; and (3) IRT from AV closure to MV opening (Figure 1). The Mod-MPI was calculated as: (ICT + IRT)/ET. Three consecutive recordings were made and the mean was considered as representative for each fetus.

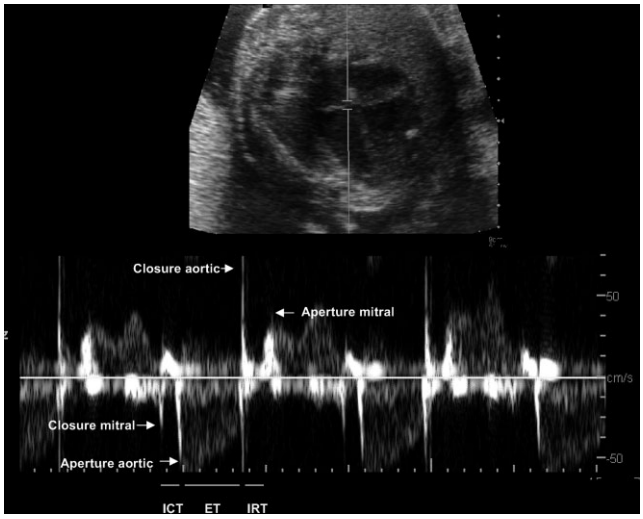

Figure 1 Apical four-chamber view of the fetal heart showing ejection time (ET), isovolumetric contraction time (ICT) and isovolumetric relaxation time (IRT). The Doppler sample gate should be located in the internal wall of the ascending aorta close to the internal leaflet of the mitral valve and below the aortic valve. The Doppler waveform shows the opening and closing 'clicks' of both valves.

For the data analysis, the SPSS 13.0 (SPSS Inc. Chicago, IL, USA) and Med Calc 7.6 (MedCalc Software Belgium) statistical packages were used. Normal distribution of the data was assessed with the Kolmogorov–Smirnoff test. To estimate the appropriate regression fit to evaluate changes in the ICT, IRT, ET and Mod-MPI in relation to completed weeks of gestation, a residual analysis was performed. The impact of fetal heart rate (FHR) on the Mod-MPI and in the three time periods was also evaluated. The 5th, 50th and 95th percentiles for each GA were calculated based on the algorithm proposed by Altman and Chitty[14], where the 5th and 95th percentiles correspond to ± 1.645 SD.

RESULTS

Throughout gestation, the Mod-MPI slightly increased (at 19 weeks it was 0.35 ± 0.027 (mean $\pm$ SD); at

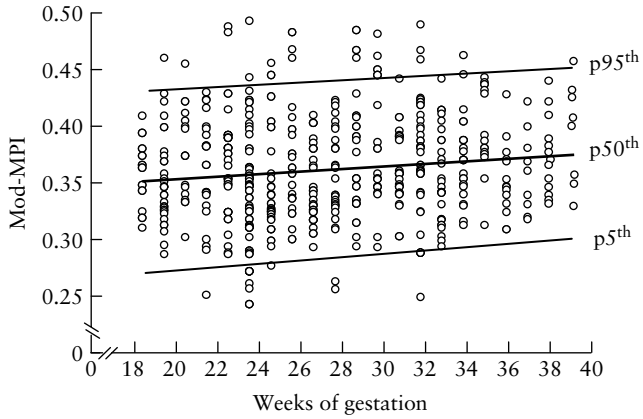

Figure 2 Plot of modified myocardial performance index (Mod-MPI) values against completed weeks of gestation. p5th, 5th percentile; p50th, 50th percentile; p95th, 95th percentile.

39 weeks, 0.37 ± 0.029; Mod-MPI $= 0.33 + 0.001 \times$ GA (weeks); $r^2 = 0.017$, Figure 2). Of the three components, ICT remained constant, IRT increased (IRT $= 0.028 + 2.52 \times$ GA (weeks)), and ET slightly decreased (ET $= 0.184 - 3.65 \times$ GA (weeks); Figure 3). The median time of MPI acquisition was 3 (range, 1–10) min. There were no differences in the distribution of values from the two institutions participating in this study.

Table 1 shows the 5th, 50th, and 95th percentiles from 19 to 39 weeks' GA. Unlike the results of other authors[11], the Mod-MPI did not exceed 0.50 at any gestational age.

Table 2 shows the effect of FHR on the three time periods and on Mod-MPI calculation. Whereas the Mod-MPI calculation did not change, ICT, IRT and ET decreased by 13–15% when FHR increased from 130 to 160 bpm.

Table 1 Normal reference values (percentiles) of the modified myocardial performance index (Mod-MPI) throughout pregnancy estimated in 557 normal fetuses

Gestational age (weeks)	*Mod-MPI*		
	5th percentile	*50th percentile*	*95th percentile*
19	0.28	0.35	0.43
20	0.28	0.35	0.43
21	0.28	0.35	0.43
22	0.28	0.35	0.43
23	0.28	0.36	0.43
24	0.28	0.36	0.43
25	0.28	0.36	0.43
26	0.28	0.36	0.44
27	0.28	0.36	0.44
28	0.29	0.36	0.44
29	0.29	0.36	0.44
30	0.29	0.36	0.44
31	0.29	0.37	0.44
32	0.29	0.37	0.44
33	0.29	0.37	0.44
34	0.29	0.37	0.44
35	0.29	0.37	0.45
36	0.30	0.37	0.45
37	0.30	0.37	0.45
38	0.30	0.37	0.45
39	0.30	0.37	0.45

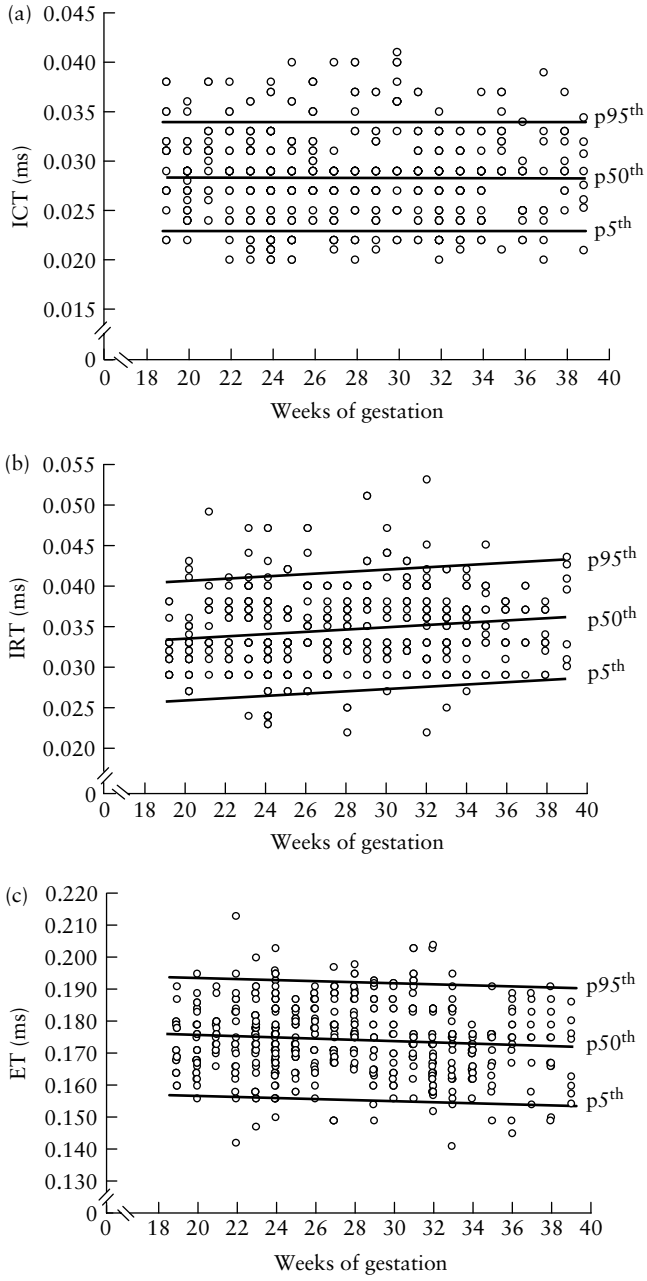

Figure 3 Plots of isovolumetric contraction time (ICT) (a), isovolumetric relaxation time (IRT) (b) and ejection time (ET) (c) against completed weeks of gestation. p5th, 5th percentile; p50th, 50th percentile; p95th, 95th percentile.

Table 3 shows a comparison of the results found in this study with previously reported normal MPI values. In general, studies using the method originally described by Tei *et al.*[6] showed higher values and standard deviations.

DISCUSSION

The results of this study demonstrate that the Mod-MPI in the left fetal heart is relatively constant throughout gestation, showing a slight increase as pregnancy

Table 2 Variations in the duration of the ejection time (ET), isovolumetric contraction time (ICT) and isovolumetric relaxation time (IRT) and in the modified myocardial performance index (Mod-MPI) in relation to fetal heart rate

Fetal heart rate	n	*ET (ms, mean ± SD)*	*ICT (ms, mean ± SD)*	*IRT (ms, mean ± SD)*	*Mod-MPI (median (range))*
160 bpm	22	148 ± 11	23 ± 4	31 ± 5	0.34 (0.31–0.40)
150 bpm	38	154 ± 10	24 ± 4	32 ± 4	0.35 (0.33–0.37)
140 bpm	42	170 ± 12	27 ± 4	36 ± 4	0.36 (0.31–0.42)
130 bpm	32	178 ± 10	28 ± 5	38 ± 4	0.35 (0.32–0.38)

Table 3 Comparison of different studies reporting normal reference values for the fetal left myocardial performance index (MPI)

Reference	n	*Approach*	*MPI (mean ± SD)*	*Comments*
Tsutsumi *et al.*[9] (1999)	50	Different Doppler waveforms	0.65; 0.43 ± 0.03*	MPI decreased during gestation
Eidem *et al.*[10] (2001)	125	Different Doppler waveforms	0.36 ± 0.06	Similar results with a higher SD
Falkensammer *et al.*[15] (2001)	23	Different Doppler waveforms	0.40 ± 0.05	Higher normal values
Friedman *et al.*[11] (2003)	74	Same Doppler waveform	0.53 ± 0.13	First study using the same waveform
Raboisson *et al.*[12] (2003)	22	Same Doppler waveform; aortic valve identification	0.37 ± 0.08	Similar results with a higher SD
Current study	557	Same Doppler waveform; aortic/mitral valve identification	0.35; 0.37 ± 0.03*	Identification of the Doppler 'clicks' of valve movements

*Mean values at 20 weeks and at the end of the pregnancy; SDs were unchanged.

advances. A low dispersion was found in the observed values, confirming previous observations that Mod-MPI has acceptable interobserver reproducibility[13].

Our results showed marked differences from those of earlier studies reporting reference values[15,16] using the methodology originally described by Tei *et al.*[7] for calculation of the MPI. The main drawback of this method is the acquisition of two different waveforms at different times, thus reducing reproducibility.

Compared with later studies, which used the same Doppler trace for MPI calculation, our values were lower than those obtained by Friedman *et al.*[11], who reported a mean MPI of 0.50. This considerable difference could be explained by the different approach used to define the time periods. In contrast, our findings are similar to those of Raboisson *et al.*[12], who used a variation of the present technique. These authors studied 22 fetuses longitudinally, reporting an MPI of 0.37 (SD 0.08), which showed no variations with GA. In our larger sample, we found a slight but constant increment in Mod-MPI values from 19 to 39 weeks (0.35 to 0.37), with a lower SD, supporting the use of GA-adjusted reference values. Interestingly, our results are similar to those observed in normal adults and in women with non-complicated pregnancies[17].

The slight elevation observed in the Mod-MPI at the end of pregnancy results from the combination of an increase in IRT and a reduction in ET. One of the manifestations of fetal cardiac maturation is the progressive increase in ventricular wall compliance, expressed as a higher relaxation capacity, and a progressive increase in the E component of the E/A waveform at advanced GA. As a result, cardiac diastolic performance improves and ejection time is reduced[18,19].

As previously reported, FHR had no effect on the Mod-MPI[7,11]. However, differences in the three time periods were observed. Calculation of the individual periods may be of clinical relevance. Some studies suggest that ICT is prolonged in the presence of hypoxia/acidemia[20] and that IRT is prolonged in pregnancy-induced hypertension[17]. Therefore, normal reference values for each time period used in MPI calculation may be useful in the investigation of different pregnancy-associated complications.

To obtain reproducible results when calculating the MPI, several methodological issues are of considerable importance. Firstly, the Doppler sample must be perfectly positioned to record the movement of the valves, allowing clear identification of the opening and closing clicks. Secondly, the fastest sweep speed available must be used to facilitate recognition of the landmarks and accurate placement of the calipers. Finally, Doppler gain must be lowered to properly identify the strong echoes of the valve clicks.

In conclusion, the Mod-MPI can be included in fetal assessment to understand cardiac adaptive changes in the presence of pregnancy-associated complications.

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