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Research Article

Differentiation of Intrauterine Growth Restriction by Myocardial Tissue Doppler

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Abstract

Introduction: Myocardial Tissue Doppler in echocardiography, which has already proved its mettle in adults and children, has also been found effective in fetal cardiac assessment. Its ability to detect cardiac dysfunction in fetuses with intrauterine growth restriction is of particular interest for better management of the condition. We undertake this study to see whether severity of intrauterine growth restriction affects the different inferences of this investigative tool.

Objectives: The objective of the study was to carry out Myocardial tissue Doppler in fetuses with differing severity of intrauterine growth restriction and observe the variations in its inferences with the same.

Design: It was a prospective observational study.

Population: Patients diagnosed with IUGR in the third trimester of pregnancy.

Methods: Myocardial Tissue Doppler was carried out in IUGR fetuses and their cardiac function evaluated.

Main Outcome Measures: The diastolic velocities at the level of both ventricles and interventricular septum (E', A', E'/A') and Myocardial performance index (MPI').

Results: There were thirty three IUGR fetuses in the study. They were found to have lower early diastolic velocity (E') and its ratio with late diastolic velocity (E'/A') at the level of the interventricular septum in comparison with thirty normal growth fetuses in significant measure.

The study subjects were classified as mild, moderate, severe and very severe degree of IUGR based on their birth weight. Three fetuses found with very severe IUGR, on comparison with normal fetuses, were found to have significantly lower Right MPI'. Five fetuses with severe IUGR had significantly lower Right and Left ventricular E'/A' along with Right Ventricular MPI'. Eleven fetuses with moderate IUGR and fourteen fetuses with mild IUGR had lower E'/A' at both interventricular septum and left ventricular level.

Conclusion: Myocardial tissue Doppler shows dysfunction in different areas of the heart in babies with different degrees of intrauterine growth restriction. Further research is needed to see its usefulness in determining the severity of and consequent urgency of intervention in IUGR.

Keywords: *Cardiac dysfunction; IUGR; Severity; Myocardial tissue Doppler*

Introduction

Tissue Doppler in echocardiography detects intrinsic myocardial tissue function. With its help, one can measure myocardial velocity in systole and diastole without the effect of transvalvular flow which is influenced by a high cardiac rate and afterload conditions. The technique processes and analyzes the Doppler frequency shift generated by Tissue movement omitting that produced by vascular flow. It has already proved to be useful in children and adults and its feasibility in fetuses has also been reported [1-3].

Cardiac function depends on myocardial contractility as well as developmental maturation, loading conditions and disease. In IUGR, the pathological process of placental dysfunction affects the different organs systems of the fetus and the cardiovascular is not an exception [4-8].

In IUGR, with decrease in the nutrient and oxygen supply due to placental vascular dysfunction, the left ventricle afterload reduces due to cerebral vasodilatation while right ventricle afterload increases due to systemic and pulmonary vasoconstriction to preferentially shift the cardiac output to increase perfusion of the brain. As hypoxia worsens, this effect deteriorates leading to impaired cardiac filling. There is also a drop in ejection fraction of both the ventricles implying that intrinsic myocardial function has also deteriorated [9].

Intrauterine growth restriction (IUGR) is a major contributor to perinatal loss and severe neonatal morbidity worldwide. In mild cases the fetus is able to cope up with this stress but in prolonged periods, it can lead to various manifestations in the various fetal organ systems with continued adaptive mechanisms that tend to get decompensated with time. This can not only lead to severe neonatal morbidities but may also have bearing upon future child and adult health too. Hence, fetuses affected with this condition need to be managed well and delivered at the correct time [10].

Serial studies on IUGR fetuses from the diagnosis of growth restriction and development of cardiac dysfunction to onset of late deceleration have led to the suggestion that an abnormal biophysical profile is a rather late phenomenon occurring in the sequence of pathophysiology of IUGR and hence can hardly be taken as the criteria for deciding on the timing of delivery for such fetuses [11]. Lookout is hence there for other tests which can detect the onset of fetal deterioration as early as possible so that intervention can be made at the correct time.

Studies on use of Myocardial tissue Doppler in this regard have seen encouraging results. The technique has shown cardiac dysfunction in IUGR fetuses in comparison to normal growth ones. IUGR however, requires a delicate balance in its management to offset the complications of prematurity while trying to prevent the ones caused by the pathology itself. Hence it becomes important to differentiate which affected pregnancies require immediate delivery and which can be continued for some time to facilitate the best outcome for the babies.

We therefore undertake the present study to see whether the severity of IUGR causes any difference in the inferences of fetal myocardial tissue doppler.

Methods

The study was done for three years in a tertiary health care centre. The Haddock's formula of calculation of the estimated fetal weight via ultrasound was used to diagnose the study subjects. On standardized custom made charts used in the hospital, the fetuses whose growth curve was below the 10^{th} percentile or showed a falling trend for their gestational age were taken for the study. Only mothers in the third trimester of pregnancy who were hence amenable for intervention were taken. The patients were explained the purpose of the study and their written consent was obtained for the same.

Sonoline Adara machine with available frequency of 3.5 MHz with specialized Sonocare software for plotting growth curves was used for imaging.

Patients with multiple gestation and fetuses with cardiac anomalies were excluded from the study as Myocardial tissue Doppler did not give tangible results in them.

Myocardial tissue Doppler through Vivid GE machine was used for the fetal echocardiography. The basal part of the both ventricular free walls and interventricular septum are the standard areas of sampling and were the points in the present study also. As Color Doppler imaging has various limitations, Spectral Tissue Doppler imaging was performed on the study and control groups of fetuses [12].

The variables of tissue Doppler are the same as in standard echocardiography denoted differently [13]:

E'-the mean peak velocity of three early diastolic waves, A'-the mean velocity of three late diastolic or atrial filling waves, E'/A'-Their ratio,

Myocardial performance index (MPI') - Deduced by ICT'+IRT'/ET' where:

ICT' - Isovolumetric contraction time,

ET' - Ejection time,

IRT' - Isovolumetric relaxation time.

The inferences were made by comparison of the variables obtained by myocardial tissue Doppler between the study and control group. SPSS software 16 was made use of for statistical analysis.

Results

Thirty three patients with IUGR constituted the study group while thirty normal growth fetuses acted as controls. Both groups have no difference in their demographic parameters except for preeclampsia which was present more in the study group. Preeclampsia is an important risk factor associated with intrauterine growth restriction and our findings affirm this [14] (Table 1).

		IUGR/Normal growth				p-value
		IUGR (33)		Normal growth (30)		
		Mean	SD	Mean	SD	
Age in years		28.10	4.74	27.22	3.70	0.974
Gestational age in weeks		33.1	0.41	34.1	0.44	0.86
		N	%	N	%	
Parity	Primi	17	53.2%	15	50%	0.901
	Multiple abortions	5	14.5%	4	13.7%	NS
	Multi	11	32.3%	11	36.3%	
Preeclampsia	Present	9	27.4%	0	0%	0.00
	Absent	24	72.6%	33	100%	sig

Table 1: *Demographic characteristics of the patients.*
Chi Square test, p value < 0.05 is significant.

Quite predictably, the IUGR fetuses had more unfavorable outcomes like Emergency Cesarean deliveries, NICU admissions, respiratory distress, early termination and low average birth weight (Table 2).

		IUGR/Normal growth				p-value
		IUGR (33)		Normal growth (30)		
		N	%	N	%	
Mode of Delivery	Vaginal	7	21.3%	16	46.7%	0.002 sig
	Elective LSCS	4	12.1%	8	26.7%	
	Emergency LSCS	22	66.6%	6	20%	
NICU Admission		18	54.5%	1	3.3%	< 0.001 sig
Respiratory Distress		5	15.1%	0	0	0.052
Hyperbilirubinemia		7	21.2%	1	3.3%	0.052
		Mean	SD	Mean	SD	
Delivery at weeks		35.58	2.8	38.4	1.16	< 0.001
Birth weight (in kg)		1.9	0.05	3	0.4	< 0.01

Table 2: *Neonatal outcomes of the patients.*
Chi Square test, p value < 0.05 is significant.

The comparison of the Myocardial tissue Doppler parameters of the study and control groups was done with the help of the independent t-test (Table 3). The parameters of IUGR babies were found lower than the control group, the Interventricular E' and E'/A' values significantly so.

	Normal growth/IUGR				p-value
	IUGR (N-33)		Normal growth (N-30)		
	Mean	SD	Mean	SD	
IV-E'	.03	0.01	.04	0.01	0.036 Sig
IV-A'	.05	0.01	.05	0.02	0.49 NS
IV-E'/A'	0.75	0.25	0.97	0.36	0.012 Sig
IV-MPI'	0.65	0.08	0.65	0.09	0.922 NS
LV-E'	0.06	0.05	0.05	0.01	0.396 NS
LV-A'	0.07	0.03	0.07	0.02	0.84 NS
LV-E'/A'	0.77	0.39	0.83	0.23	0.46 NS
LV-MPI'	0.63	0.16	0.65	0.12	0.60 NS
RV-E'	0.08	0.013	0.07	0.02	0.47 NS
RV-A'	0.09	0.02	0.10	0.02	0.23 NS
RV-E'/A'	0.60	0.23	0.70	0.19	0.10 NS
RV-MPI'	0.67	0.19	0.68	0.12	0.66 NS

Table 3: *Myocardial tissue doppler parameters among IUGR and normal growth babies as a whole group.*
Test used: Independent t test, p value < 0.05 considered significant. Values: E', A' in m/sec, E'/A' and MPI' are ratios.

For the purpose of the study, the babies with IUGR were classified on the basis of severity assessed by their birth weight:

1. Very severe IUGR-(Birth weight < 1 kg)-3
2. Severe IUGR-(Birth weight < 1.5 kg)-5
3. Moderate IUGR-(Birthweight-1.5 - 2 kg)-11
4. Mild IUGR-(Birth weight-2 - 2.5 kg)-14.

The very severe IUGR babies too repeated the pattern of lower parameters than normal growth babies (Table 4). Only the right ventricular parameter MPI' was statistically significant. Severe IUGR babies had significantly lower Left and Right ventricular E'/A' along with Right Ventricular MPI' than normal growth babies.

	Very Severe IUGR (N-3)		**Normal (N-30)**		**p-value**
	Mean	**SD**	**Mean**	**SD**	
RV-E'	0.06	0.01	0.07	0.01	0.62 NS
RV-A'	0.08	0.01	0.09	0.03	0.61 NS
RV-E'/A'	0.69	0.10	0.72	0.21	0.87 NS
RV-MPI'	0.47	0.04	0.72	0.14	0.04 Sig
	Severe IUGR (N-5)		**Normal (N-30)**		
LV-E'/A'	0.84	0.16	0.87	0.22	0.01 Sig
RV-E'/A'	0.43	0.07	0.72	0,21	0.02 Sig
RV-MPI'	0.49	0.23	0.72	0.14	0.04 Sig
	Moderate IUGR (N-11)		**Normal (N-30)**		
IV-E'/A'	0.60	0.20	0.97	0.44	0.03 Sig
LV-E'/A'	0.59	0.22	0.87	0.22	0.01 Sig
	Mild IUGR (N-14)		**Normal (N-30)**		
IV-E'/A'	0.60	0.20	0.97	0.44	0.03 Sig
LV-E'/A'	0.59	0.22	0.87	0.22	0.01 Sig

Table 4: *Comparison of myocardial tissue doppler parameters with severity of IUGR.*
Test used: Independent t test, p value < 0.05 considered significant. E', A' in m/sec, E'/A' and MPI' are ratios.

Both the mild and moderate IUGR babies showed significantly reduced Interventricular and Left ventricular E'/A' than the control group.

Discussion

Tissue Doppler in echocardiography as an investigative modality was first described in 1989.In adults, this technique can identify subtle cardiac dysfunction in preclinical stages and hence it acts as a prognostic tool in major cardiac diseases, such as heart failure, acute myocardial infarction, and hypertension.

The method uses the high amplitude and low frequency signals generated by the myocardial tissue while movement during the cardiac cycle without being biased by the load conditions [15]. The different factors made note of are myocardial velocity, myocardial velocity

gradient, myocardial strain and strain rate. The technique thus can enable us to identify if there is actual cardiac dysfunction or just altered functioning as a compensation to tide over unfavorable circulatory changes, a common situation in intrauterine growth restriction.

Tissue Doppler in fetal cardiac assessment has reported interesting results. On measuring at the level of the left ventricular posterior wall, right ventricular anterior wall and interventricular septum in fetuses between 19 - 38 weeks, Harada and associates observed a gestational age specific increase in the peak myocardial velocities during early diastole and atrial contraction in both the ventricles [1].

Elmstedt., *et al*. found similar findings [16]. They also observed that there was a longitudinal shortening of the fetal myocardium with gestational age most likely due to a physiological change as preload is stable and afterload declines with advancing gestational age ruling them out as causes. Hence a conclusion was made that cardiac muscle contractility in the human fetus decreased with gestational age.

Gardiner., *et al*. ffound that myocardial tissue Doppler is a better predictor of myocardial function than conventional Doppler in diagnosing the maturational changes occurring in fetal systole and diastole function as well as the velocities in both ventricles despite differential loading conditions [17].

On standard echocardiography, IUGR fetuses show impaired ventricular filling, lower peak velocities in the major arterial vessels and a relative increase in left over the right cardiac output. With serial recordings, the ratio of left to right ventricular outputs tend to remain stable in IUGR fetuses, suggestive of no significant increase in outflow resistance or cardiac output redistribution after establishment of the brain sparing mechanism. However, the absolute values tend to decline rather than increase with gestational age as is normally seen due to decrease in the myocardial ejection force. Perhaps with time, further deterioration of the fetal condition if the underlying insufficiency is not corrected, undermines the protective mechanisms of the dilatation of the peripheral circulation [18].

Different studies undertaken to see the performance of Myocardial tissue Doppler in IUGR fetuses have found variable results reflective of these changes. Watanbe., *et al*. found that the ratio of the systolic velocities in both ventricles is higher in IUGR fetuses and lower in hydrops babies than normal growth ones [19]. Naujorks., *et al*. found higher diastolic velocity ratio at the level of the left ventricle and the septum and lower ratio of standard early diastolic velocity to tissue Doppler velocity at the left ventricle in IUGR babies than normal ones [20]. Comas., *et al*. through their findings stated that the diastolic ratios and global cardiac function values were higher at all levels in early IUGR [21] while a study by Larsen., *et al*. showed a lower left and right A' in addition to higher left diastolic velocity ratio like Naujorks in IUGR [22].

In contrast to their previous study, Comas., *et al*. found a lower E' and A' only in the right ventricle along with a higher MPI' at all levels in 58 IUGR fetuses [23]. A study conducted by the authors with a similar sample size showed a subtle right sided cardiac dysfunction in IUGR fetuses than normal growth fetuses [24].

Niewiadomska-Jarosik., *et al*. took the initiative one step further by conducting the study in 77 children aged 5 - 11 years. In the group of children with IUGR in their fetal life, at all levels the E wave and E/A ratio were significantly lower and A wave, isovolumetric relaxation time, deceleration time, MPI' were significantly higher. Also higher were the ratios of standard echocardiographic values at early diastole with the tissue Doppler values [25]. This study gives credence to the Barker's hypothesis by demonstrating the persistence of myocardial dysfunction of IUGR beyond the fetal life.

The diagnosis of intrauterine growth restriction is almost impossible without reliable dating. Due consideration was taken in our study by choosing only patients with excellent or good dating. So the chances of our data being affected by false categorization were nil. The demographic characteristics in both our groups were also similar removing any other factors than IUGR leading to a difference in the changes observed. Inter and intra observer variations were also avoided by carrying out the imaging by the same person on the same machine.

Preeclampsia is a risk factor found in association and also postulated for the causation for the development of intrauterine growth restriction. This fact is also proved in our study with nearly 30% of our cases suffering from the condition [14].

Our findings of all Myocardial tissue Doppler parameters to be lower in all the babies with IUGR than those with normal growth suggest an overall reduction in the level of effective cardiac function as was also exhibited on standard echocardiography. The parameters significantly reduced were of the interventricular septum which is an area most susceptible to hypoxia due to its low circulatory supply and hence most affected due to the underlying pathology.

Conducting our study on the lines of our main objective, i.e. comparison of Myocardial tissue Doppler parameters on the basis of the severity of IUGR brought us interesting observations. While in mild and moderate IUGR, the interventricular septum and left ventricle are most affected, in severe IUGR both the ventricles appear to be bearing the brunt. In very severe IUGR, the right ventricular global function represented by the Myocardial performance Index is heavily affected. Due to dependence on placental circulation for supply of oxygen and nutrients, the right side of the heart which acts as a conduit for its passage to the different organ systems takes a more dominant role in fetal life. As a result this is the area more in requirement of oxygen and nutrients and unable to adapt to the increasing pathophysiology of placental dysfunction. This therefore explains the observation of right sided parameters to be abnormal with IUGR [26].

These different findings, probably explained by the adaptive mechanism of the fetal myocardium with increasing severity of IUGR can help in differentiating the babies which require urgent intervention in the form of delivery from the ones which can be allowed some more time intrauterine to prevent immaturity. Our study gives an affirmation in this direction and more research is needed in this regard.

A major limitation of our study was the varying sample size as due to fetal compromise necessitating immediate delivery, a small amount of very severe IUGR babies could be taken for the study. Also, the myocardial dysfunction detected by the imaging could have got more credence if Troponin T levels of these babies could have been calculated. However, as the study subjects were in their fetal stage, due to improper crossing of this compound through the placental barrier, it would not have produced conclusive results [27].

IUGR leaves devastating consequences in the babies it affects, as seen also in our present study group. Techniques that can help differentiate the severely afflicted babies from the milder ones can reduce the morbidities associated with prematurity and the pathology itself. More research is needed to see if Myocardial Tissue Doppler is the right answer to this quest.

Conclusion

Myocardial tissue Doppler shows dysfunction in different areas of the heart in babies with different degrees of intrauterine growth restriction. This indicates that different areas of the fetal heart are affected with increasing severity of IUGR. Further research with more sample size is needed to see its usefulness in determining the severity of and consequent urgency of intervention in IUGR.

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Conflict of Interest

None.

Ethical Approval

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