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Original Research Article

Can Myocardial Tissue Doppler Predict Neonatal Outcome?

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Abstract:

Objective: Intrauterine growth restriction (IUGR) is associated with numerous neonatal complications in the affected fetuses. We undertook this study to assess whether myocardial tissue Doppler, found to detect subclinical cardiac dysfunction in IUGR, is an effective tool in predicting the neonatal outcome.

Materials and Methods: It was a prospective cohort study in a teaching hospital conducted on fetuses affected by IUGR. Cardiac function was evaluated with the help of Myocardial Tissue Doppler (Right and Left Ventricular and Interventricular septal E', A, E'/A' and Myocardial performance index (MPI')) and correlated with their neonatal outcomes.

Results: Among the sixty-two fetuses taken, there were 3 mortalities, two developed cardiomegaly and fifteen developed respiratory distress. Right ventricular MPI' was found significantly reduced in fetuses with adverse neonatal outcomes. Fetuses with adverse neonatal outcomes had both abnormal conventional vessel and myocardial tissue Doppler while significant number of fetuses with normal outcomes only had abnormal myocardial tissue Doppler. Right ventricular MPI' had sensitivity of 40 % in detecting adverse neonatal outcomes and of 60% in detecting fetuses with normal outcomes.

Conclusion: Myocardial tissue Doppler has good sensitivity in predicting normal neonatal outcome in fetuses with IUGR. It is however not a sensitive indicator of adverse outcome in IUGR in comparison to conventional vessel Doppler.

Keywords: IUGR, Myocardial tissue Doppler, Neonatal outcomes, Respiratory Distress.

Introduction

Many fetuses with IUGR have poor immediate condition at birth [1], the ones with fetal compromise diagnosed by Doppler and/or biophysical profile more at risk [2]. Certain neonatal morbidities tend to be more specifically associated with IUGR [3]. Poor glycogen reserves and metabolic adaptation lead to poor tolerance of hypoxia and higher incidence of birth asphyxia and meconium aspiration syndrome. Low IGF-I, glucose, insulin, albumin and cholesterol levels and elevated levels of lactate and non-esterified fatty acids are found increasing the risk for neonatal hypoglycemia, the highest incidence in the first 24 hours [4].

The decreased left ventricle and increased right ventricle afterload at first progressively deteriorates causing reverse flow in inferior vena cava and atrial contraction and reducing end diastolic velocity in the umbilical vein manifested as end-diastolic pulsations frequently associated with acidemia and endocrine changes. If not delivered by then, intrauterine death ensues [5]. There is consequent ischemia to muscles, kidney and gut leading to high incidence of necrotizing enterocolitis. Some studies demonstrate an excess of RDS in SGA babies with timing of delivery and administration of steroids a confounding factor [6,7,8]. IUGR has been inconsistently associated with higher incidences of interventricular haemorrhage and periventricular leukomalacia.

Myocardial tissue Doppler ultrasonography constitutes processing and analyzing the Doppler frequency shift (after filtering out the high frequency blood flow signals) generated by Myocardial Tissue movement to accurately look at the tissue function [9]. In adults and children, it has been demonstrated to be useful in prediction of future cardiovascular diseases. Studies done so far postulate the feasibility and sensitivity of tissue Doppler in fetuses with IUGR [10-16]. We

undertake the present study to see if Myocardial tissue Doppler can predict the adverse neonatal outcomes of this condition.

Materials and Methods

It was a prospective observational cohort study, carried out for a period of three years, in a hospital providing care at tertiary level. All patients in the third trimester of pregnancy admitted with the diagnosis of intrauterine growth restriction (Growth of fetus below the 10th percentile for their gestational age) in this period were taken for the study [17]. Patients were explained about the study and written consent was taken from all of them.

Patients with multiple gestation and fetuses with diagnosed cardiac anomalies were excluded from the study as it is difficult to perform the technique on them.

Fetal echocardiography was done along with myocardial tissue Doppler in all these patients with help of Vivid GE machine. The standard areas of fetal echocardiography i.e., the basal part of the left ventricular free wall, right ventricular wall and interventricular septum of the fetal heart were taken for the measurements.

E' (average maximum velocity of early diastolic waves), A' (average maximum velocity of late diastolic or atrial filling waves), E'/A'-Their ratio and the Myocardial performance index (MPI') - ICT'+IRT'/ET' (ICT' - isovolumetric contraction time, ET' - ejection time, IRT' -isovolumetric relaxation time) were the tissue Doppler variables of the myocardium considered.

The fetuses were also subjected to conventional vessel Doppler at the level of the umbilical artery, middle cerebral artery, and ductus venosus. All neonates were followed up to 7 days post-delivery. Hypoglycemia, respiratory distress syndrome, presence of cardiomegaly, neonatal seizures and mortality were taken as the major adverse neonatal outcomes for our study.

All the statistical analyses were done with the help of SPSS software 16.

Results

Sixty-two patients with IUGR were found eligible in the three-year period of the study. Twenty-six of these fetuses required prolonged NICU admission post-delivery however only fifteen had severe complications of respiratory distress requiring ventilator care. Among them, nine were found to be asphyxiated at birth, five also acidotic. Three fetuses died, one of pulmonary hemorrhage and another of cardiac failure post-delivery. In the case of the 3rd fetus, in view of poor prognosis the mother refused any intervention leading to intrauterine death. Six babies developed hyperbilirubinemia requiring phototherapy which is a common physiological phenomenon seen also in normal growth fetuses so this was not considered an adverse outcome [18]. Other adverse neonatal outcomes like hypoglycemia and cardiomegaly were not found in significant number.

The fetuses were divided into two groups based on the development of neonatal morbidity:

1. IUGR fetuses with neonatal morbidity-Fifteen in the present study

2. IUGR fetuses with normal outcomes-Forty-seven in the present study

On comparing these two groups with regards to myocardial tissue Doppler, the right ventricle Myocardial performance index was significantly lesser in babies who developed severe morbidity. This probably indicates the presence of right ventricular dysfunction in IUGR babies who develop adverse neonatal outcomes (Table 1).

As there is no defined cut-off yet for fetuses for these parameters, the sensitivity of this variable in predicting adverse outcomes was assessed with Correlation curves. A negative correlation of Right MPI' was found with adverse neonatal outcomes. Lower the myocardial performance index, worse is the outcome of the fetus (Figure 1). However, the sensitivity as per the curve obtained is only 40% at a cut-off value of 0.65. Hence this value is likely to miss a lot of patients with adverse neonatal outcomes.

Similar finding was obtained when correlation curve was attempted for another variable of Right ventricular A' with a sensitivity of 40% at a cut-off value of 0.095m/sec (Figure 2).

The findings obtained with myocardial tissue Doppler were compared to the findings obtained through Conventional Vessel Doppler, to see which of the two was more sensitive in predicting adverse neonatal outcomes. As there are no fixed cut-offs for myocardial tissue Doppler, the ones obtained by these curves were used for this purpose.

Among all the fetuses taken for the study, abnormalities were more found in Umbilical artery Doppler values in twenty-seven of them like raised indices, absent or reversed end diastolic flow. Middle cerebral artery Doppler values were also altered in 5 of these fetuses while no abnormalities were found in Ductus venosus waveforms in any of the study subjects. Among the fifteen babies with neonatal morbidity both conventional Vessel Doppler (11) and Myocardial tissue Doppler (12) values were equally abnormal. There was no statistically significant difference between the two.

However, when the cut-off for Myocardial Tissue Doppler was applied to IUGR babies with normal outcomes, there were still significant number of babies with abnormal values unlike Vessel Doppler

which remained normal for these babies. Hence Conventional Vessel Doppler was more sensitive than myocardial tissue Doppler in accurately predicting babies with adverse neonatal outcomes (Table 2). Among the Twenty-seven fetuses with IUGR and abnormal vessel Doppler, nineteen had values less than the defined cutoff values as per the sensitivity curves, i.e. an abnormal myocardial tissue Doppler. Eleven out of them had adverse neonatal outcome. Five fetuses had serious outcomes of birth asphyxia and acidosis (cord pH < 7.2) and one died intrauterine. They all had abnormal Myocardial tissue Doppler variables with reduced right ventricular Myocardial performance index and A' (Table 3).

When sensitivity of Myocardial tissue Doppler was checked in normal outcome fetuses, it was found that Right ventricular Myocardial Tissue Doppler had better sensitivity in predicting normal neonatal outcomes than adverse (Figure 3). The variable shows a positive correlation with normal neonatal outcomes. The sensitivity also is appreciable around 60% with a cutoff of 0.6. Patients with values higher than this would have normal neonatal outcome. A significant number of IUGR fetuses who were thus ascribed to have normal Myocardial tissue Doppler had normal neonatal outcomes. Very few fetuses with adverse outcomes were described to have normal myocardial tissue Doppler using this cutoff. (Table 4). Among the neonates with asphyxia at birth the average Right ventricle Myocardial performance Index and the average Left ventricular Myocardial performance Index was lower than the average values obtained for all the IUGR fetuses more so for right ventricular myocardial performance index which is consistent with the findings obtained as for the present study (Table 5). The myocardial tissue Doppler findings of all the study subjects were compared with 58 suitably matched normal growth controls without any adverse neonatal outcomes. All study subjects had subtle right ventricular myocardial dysfunction as has been found in many studies.

As per the findings of the present study, Myocardial tissue Doppler shows is a sensitive investigative modality in predicting normal neonatal outcomes in IUGR. It however is not a more sensitive predictor of adverse neonatal outcomes than conventional vessel Doppler.

Table 1: Myocardial tissue parameters among IUGR babies who developed morbidities and those with normal outcomes:

	IUGR				p-value
	Morbidity(N-15)		Normal Outcome (N-47)		
	Mean	SD	Mean	SD	
IV-E'	0.04	0.0078	0.039	0.01	0.85
IV-A'	0.05	0.13	0.49	0.13	0.64
IV-E'/A'	0.81	0.33	0.85	0.30	0.52
IV-MPI'	0.61	0.10	0.62	0.09	0.68
LV-E'	0.05	0.017	0.055	0.027	0.49
LV-A'	0.066	0.023	0.068	0.022	0.73
LV-E'/A'	0.80	0.36	0.80	0.28	0.99
LV-MPI'	0.628	0.17	0.647	0.11	0.59
RV-E'	0.06	0.01	0.07	0.007	0.56
RV-A'	0.09	0.017	0.09	0.02	0.14
RV-E'/A'	0.63	0.15	0.62	0.24	0.93
RV-MPI'	0.59	0.16	0.65	0.13	**0.05**

Test used: Independent t test, p value <0.05 considered significant. E', A' in m/sec, E'/A' and MPI' are ratios. Values in m/sec

Table 2: Efficacy of Conventional Vessel Doppler and Myocardial Tissue Doppler in detecting IUGR babies with adverse neonatal outcomes

	IUGR babies with morbidity (15)	IUGR babies with normal outcome (47)	p Value
Abnormal Vessel Doppler	11	16	0.05
Normal Vessel Doppler	4	31	
Abnormal Myocardial tissue Doppler	12	28	0.21
Normal Myocardial Tissue Doppler	3	19	

Test used: Chi Square test, p Value <0.05 considered significant

Table 3: Compilation of vessel Doppler and Myocardial tissue Doppler parameters in babies with serious neonatal outcomes:

Baby	Adverse outcome	Vessel Doppler	Myocardial Tissue Doppler
1	Cardiomegaly, Birth asphyxia, acidosis, and mortality	Raised indices	Reduced Right Ventricle MPI'
2	Cardiomegaly	Absent end diastolic flow	Reduced Right Ventricle MPI'
3	Birth Asphyxia and acidosis	Absent end diastolic flow	Reduced Right Ventricle MPI' Reduced Right Ventricular A'
4	Birth Asphyxia and acidosis and mortality	Absent end diastolic flow	Reduced Right Ventricle MPI'
	Birth Asphyxia and acidosis	Reversed end diastolic flow	Reduced Right Ventricle MPI' Reduced Right Ventricular A'
5	Birth Asphyxia and acidosis	Normal Vessel Doppler	Reduced Right Ventricle MPI'
6	Intrauterine fetal death	Reversed end diastolic flow	Reduced Right Ventricle MPI' Reduced Right Ventricular A'

Table 4: Efficacy of Myocardial Tissue Doppler in detecting IUGR babies with normal neonatal outcomes

	Abnormal Myocardial tissue Doppler	Normal Myocardial Tissue Doppler	p Value
IUGR babies with morbidity (15)	12	3	0.012
IUGR babies with normal outcome (47)	11	36	

Test used: Chi Square test, p Value <0.05 considered significant

Table 5: Average Myocardial performance index in babies with perinatal asphyxia in comparison to the mean myocardial performance index in all IUGR babies:

	Right Ventricular MPI'	Left Ventricular MPI'	p Value
IUGR babies with birth asphyxia	0.59+/-0.16	0.61+/- 0.20	1.9 NS
All IUGR babies	0.63+/-0.12	0.62+/-0.16	

Test used: Chi Square test; Values in m/sec

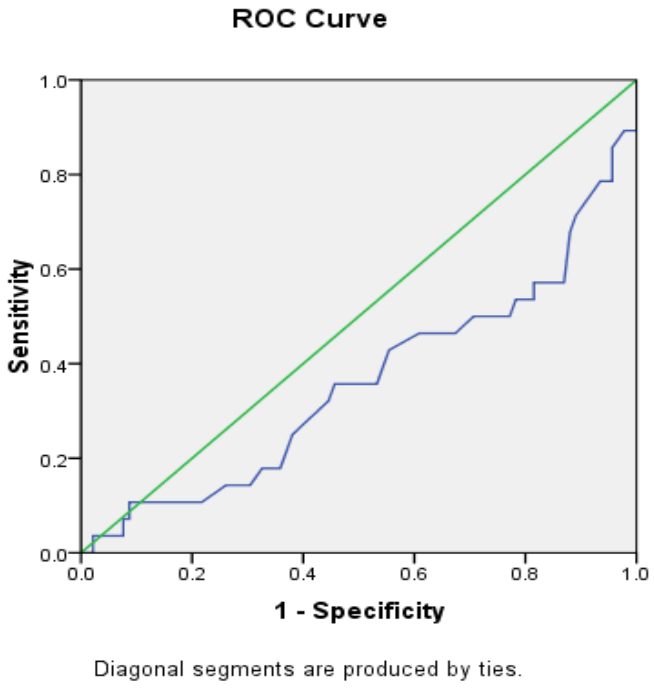

Figure 1: Sensitivity curve of Right Ventricular Myocardial Performance Index in predicting adverse neonatal outcomes: (Values in percentage as MPI' is a ratio)

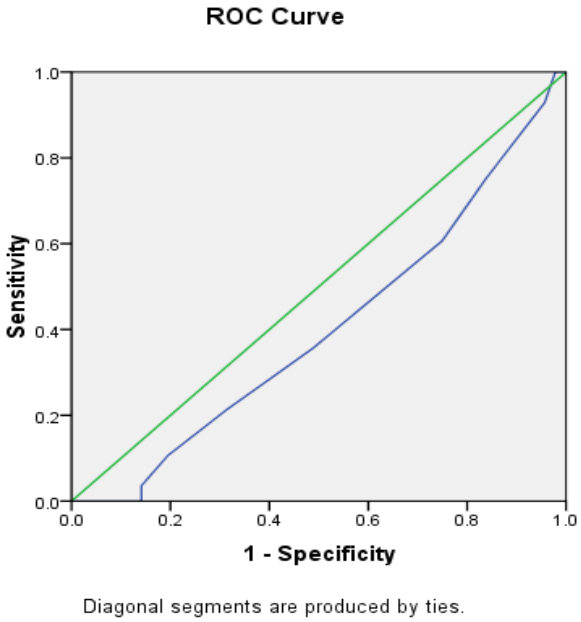

Figure 2: Sensitivity curve of Right Ventricular A' in predicting adverse neonatal outcomes: (Values in m/sec)

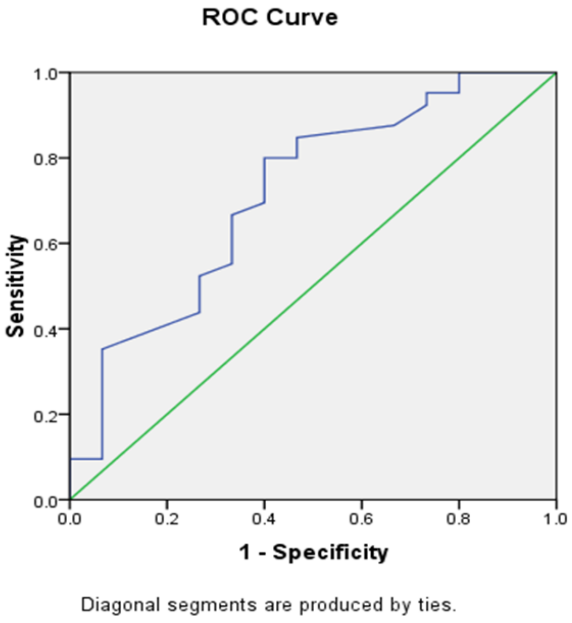

Figure 3: Sensitivity curve of Right Ventricular Myocardial Performance Index in predicting normal neonatal outcomes: (Values in percentage as MPI' is a ratio)

Discussion

Intrauterine growth restriction affects 5-10% fetuses all over the world. It is associated with morbidities affecting the different fetal organ systems consequent to the adverse effects of the underlying pathology of placental dysfunction that have both immediate and far reaching results[1,3,6,7,8]. The management of this condition is quite tedious and resource consuming leading to a global economic burden so any investigative modality that aids in this regard will be of great help especially in developing countries. An investigative tool that can predict which IUGR fetuses are at more risk of adverse perinatal and neonatal outcomes can help in triaging them and enable more vigorous and efficient treatment.

Myocardial Tissue Doppler has been proven to detect cardiac dysfunction in IUGR fetuses in many

case control studies [13,14,15,16]. Our aim was to see if it can further differentiate between the fetuses requiring more energetic measures and the ones not and whether it is better in this regard then the already existing method of conventional vessel Doppler. As is found in most studies our subjects overall had cardiac dysfunction on comparing them with a group of normal growth fetuses.

No remarkable variation in the Myocardial Tissue Doppler parameters were seen with increasing gestational age among the fetuses allotted for the study. These rules out any effect of gestational age on our observations. This is further proved on not finding similar changes in the normal fetuses. The studies showing differences in Myocardial Tissue Doppler with gestational age have usually recruited patients in both second and third trimesters whereas we have only taken third trimester patients [19,20].

In fetal life it is the right side of the heart which plays the dominant role in the circulation of blood [21]. As a result, this is the area to be more in requirement of oxygen and nutrients and less adaptable to hypoxia and ischemia. This correlates well with our findings of Right ventricular parameters to be affected more in fetuses who developed severe neonatal morbidities.

In present literature, ours is the only study that has tried to corelate Myocardial tissue Doppler findings with immediate neonatal outcomes in fetal growth restriction. Studies which have tried to assess the observations of Tissue Doppler in the neonatal or early childhood have either tried to reproduce the findings of fetal cardiac dysfunction of growth stunting or define the structural changes of the cardiovascular system in response to the extrauterine environment after birth. Wosiak et al found subclinical cardiac dysfunction persisting in babies born with intrauterine growth restriction in their fetal life [22].

Studies by Fouzas et al [23] and Rodriguez-Guerineau et al [24] found both cardiac structural and functional changes in neonates with IUGR on comparison with those with growth appropriate for gestational age like interventricular septal hypertrophy, mild left ventricular dilation, higher left stroke volume and lower early diastolic velocities at the level of the septal annulus. These changes became the basis for predicting the risk of developing hypertension and cardiovascular risk factors at an early age in such infants in a study by Cruz-Lemini et al [25]. They found the tricuspid annular plane systolic excursion an important index along with the cerebroplacental ratio and interventricular relaxation time in the prognostication of infant hypertension and arterial remodelling in IUGR fetuses. These are however, long term outcomes which can only be reached at successfully if the immediate sequelae of the pathology of growth restriction can be managed efficiently in affected babies. Wei et al demonstrated left ventricular systolic function in new born babies with birth asphyxia with decrease in the peak annular mitral valve velocity constant even after 48-72 hours at birth [26]. But the study was conducted in normal growth newborns and did not assess any predictive value of Tissue Doppler for this negative outcome. Even though our study population is different, the babies with birth asphyxia in our study also showed a drop in global cardiac function over those with normal neonatal outcomes.

Tejaswi et al attempted a similar study as ours among fetuses of diabetic mothers [27]. Though they found significant myocardial hypertrophy persisting in neonatal life particularly in poorly controlled diabetics but there was no corelation of Myocardial Tissue Doppler with perinatal outcomes.

There are no other studies comparing the sensitivity of Conventional vessel Doppler in predicting neonatal outcomes with that of Myocardial tissue Doppler but there are some demonstrating the superiority of the latter in detecting cardiac dysfunction in IUGR fetuses over the former[14,28].In our study vessel Doppler is adjudged a more sensitive investigation in predicting adverse neonatal outcomes but the findings of abnormal tissue Doppler in babies with normal outcomes may have a different connotation. The presence of abnormal tissue Doppler in babies with no serious outcomes may indicate subtle cardiac dysfunction not translating into adverse sequelae. It may also imply, as also denoted by the Cruz-Lemini study that these fetuses are at increased risk of developing hypertension and other cardiovascular diseases in the future and they should be kept under observation for early diagnosis and treatment [24].

One limitation of our study was that many fetuses with reversed end diastolic flow or very severe growth restriction could not be included on account of them mostly referred with severe distress necessitating immediate delivery. Further research on such fetuses can help in finding out stronger cut off values with higher sensitivity.

Confirmation of cardiac dysfunction with Troponin T could not be done in our study which could have proved the decompensated cardiac function biochemically. Cardiac Troponin T is a thin filament protein present in myocardial fibers which are released in the event of serious myocardial injury in the circulation. In adults on account of its cardio-specific nature it has been made use of in the diagnosis of myocardial infarction. Hence its elevation in fetuses also definitely indicates the presence of myocardial injury and hence cardiac dysfunction in them. However a study by Crispi et al to look at cardiac dysfunction across the various stages of Doppler deterioration in IUGR showed no

significant increase in the levels of Troponin T in IUGR fetuses with Doppler abnormalities in comparison to other markers like Atrial natriuretic peptide, Blood B-type Natriuretic peptide, C reactive protein[29].The marker was found elevated to a significant extent only in babies who died indicating the presence of severe myocardial injury only in babies with severe hemodynamic alterations. Since most of the babies taken in our study did not have very serious Doppler changes the cardiac Troponin levels may not have been elevated to an appreciable extent even though they were found to have abnormal myocardial tissue Doppler.

Though the low sensitivity of Myocardial tissue Doppler in forecasting adverse neonatal outcomes runs the risk of panic and waste of resources in the management of IUGR fetuses with ultimately uneventful consequences, its high specificity in this regard and subsequent greater sensitivity in predicting normal outcomes helps in the prognostication of the IUGR fetuses and segregation and efficacious allotment of measures in their delivery and handling of the sequelae thereafter.

Further research in this direction can help develop this investigative modality into a method of great aid in the treatment of IUGR and its complications. As per our observations, the measure doesn't replace conventional vessel Doppler for this purpose rather acts as an adjunct to it by pinpointing the exact area of cardiac dysfunction.

Conclusion

We conclude that Myocardial tissue Doppler has good sensitivity in predicting normal neonatal outcome in fetuses with IUGR. It is however not a more sensitive indicator of adverse perinatal outcome in IUGR babies than conventional vessel Doppler.

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