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RESEARCH ARTICLE

GOAL DIRECTED THERAPY USING FUNCTIONAL ECHOCARDIOGRAPHY

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ABSTRACT

The clinical assessment of circulatory adequacy has been shown to be inaccurate in term and preterm infants (Tibby *et al*., 1997 and Osborn *et al*., 2004). Functional echocardiography, by treating Neonatologists, gives noninvasive insight into the hemodynamic status of patients quantitatively and helps in guiding treatment strategies accordingly. In this article, we will elaborate case scenarios where functional echocardiography decisively helped in the management of patients.

INTRODUCTION

In the sick and preterm neonate, there is a delay in adaptation from fetal system to neonatal system of circulation which occurs usually in the first 48 hours of life. This transitional circulatory changes. It can be abnormal in following ways: (1) delay in the rapid increase in the cardiac output (left ventricle has to double its output) (Kluckow and Evans, 2001) against sudden increase in systemic vascular resistance (2) persistence of ductus arteriosus (3) delay in the physiological fall in the pulmonary vascular resistance (Kluckow and Evans, 2001; Kluckow, 2005 and Skinner *et al*., 1992). Quantitative assessment using functional echocardiography will help in finding the most physiologically relevant therapy during this time. Functional echocardiography refers to bedside echocardiography by non-Cardiologist for real time assessment of the myocardial function, pulmonary or systemic hemodynamics, and ductus arteriosus, which addresses a specific clinical question or management dilemma. In this article, we present clinical scenarios where functional echocardiography enabled appropriate therapeutic decisions. We shall discuss the most appropriate techniques in terms of echocardiographic views, measurement methods for each of these scenarios according to the latest literature. Echocardiographic evaluations were performed by a single neonatologist at Tertiary Neonatal Intensive Care Unit, India, who received comprehensive training from Pediatric Cardiologists. All findings were recorded and confirmed with the Pediatric Cardiologist for quality assurance.

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Review of cases

Case scenario I

A 28 week preterm neonate, with history of leaking per vaginum for more than 48 hours, weighing 1575 g was intubated and mechanically ventilated in neonatal intensive care unit (NICU) and given surfactant at birth. Although the compliance improved, the neonate had persistent hypoxia with oxygenation index of more than thirty, hence High frequency oscillatory ventilation was started. Chest X-ray was suggestive of consolidation. Echocardiography was done by the neonatologist, which showed features suggestive of severe pulmonary hypertension which includes:

Parasternal short axis view: Ductus arteriosus 3.5mm with reversal of shunt (3 legged stool sign).

Parasternal short axis view: Time to peak velocity or Acceleration time in pulmonary arterial blood flow in pulsed wave mode was 20ms (Fig. 1) and the ratio of Time to peak velocity to Right ventricular ejection time was less than 0.34. (Time to peak velocity or Acceleration time is defined as the interval between the onset of systolic pulmonary arterial flow and peak flow velocity. Value less than 80 ms is taken as a marker of pulmonary hypertension (Yared *et al*., 2011; Kitabatake *et al*., 1983 and Skinner *et al*., 2000). Similarly, ratio of Time to peak velocity to Right ventricular ejection time less than 0.34 taken as a marker of pulmonary hypertension (Evans *et al*., 1998 and Skinner *et al*., 2000). Right Ventricular ejection time is defined as the interval

between the onset of Right ventricular ejection to the point of systolic pulmonary arterial flow cessation)

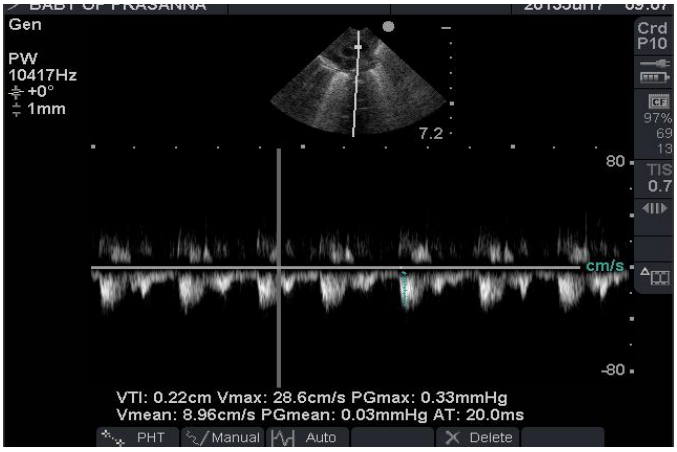

Fig.1. Parasternal short axis view showing Time to peak velocity/ Acceleration time 20ms

Apical view: TR jet with peak velocity was 4m/s in continuous wave mode. This gives a right ventricular systolic pressure of 69mmHg (4 X velocity^2 + 5 mmHg) (Skinner *et al*., 2000; Skinner *et al*., 1993 and Skinner *et al*., 1992) which was more than systemic systolic pressure (suprasystemic) Right ventricle was globular with bowing of interventricular septum in to the left ventricle (Fig. 2).

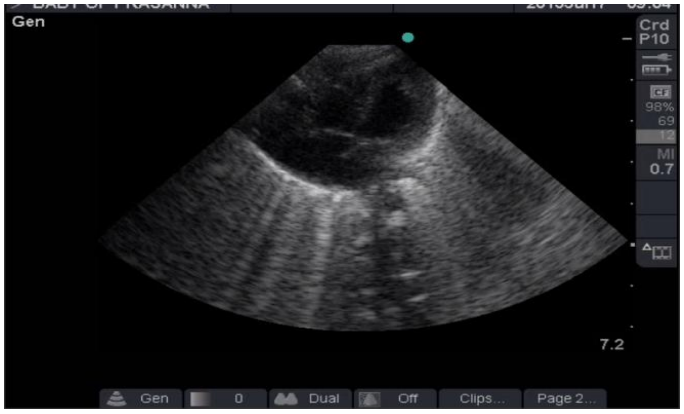

Fig. 2. Apical 4 chamber view: globular right ventricle with interventricular septum shifted to the left ventricle

We started sildenafil (1mg/kg/dose 6 hourly) (Baquero *et al*., 2006), and milrinone (0.5 microgram/kg/min) (McNamara *et al*., 2006). On day 3, repeat echocardiography showed that pulmonary pressure are moderately elevated but not suprasystemic. Ductus arteriosus was showing features suggestive of hemodynamic significance, which includes:

Short paraternal view: Ductal dimension at the point of maximum constriction more than 1.5mm.

Parasternal long axis view: On M mode, left atrium to aortic ration more than 1.4 (Sehgal and McNamara, 2009; Iyer and Evans, 1994 and Silverman *et al*., 1974).

We tapered and stopped milrinone and started Iburufen (Sehgal and McNamara, 2009) course for the closure of the ductus arteriosus. The ductal status was monitored using echocardiography. After 2 days of starting Ibuprofen the ductus was closed. Longitudinal echocardiographic assessment by the treating neonatologist helped in the detection of initially severe persistent pulmonary hypertension of newborn which responded to appropriate management and then due to shunt reversal became a hemodynamically significant PDA.

Case scenario II

A 28 week preterm neonate weighing 880g was born to a primigravida mother by Cesarian section in view of preeclampsia delivery. The neonate was having mean blood pressure of 23 mm Hg at 2 hours of life by noninvasive blood pressure. Although as per gestation of neonate suggested that the blood pressure should be more than 28mmHg (Development of audit measures, 1992). Echocardiography showed that cardiac contractility, by fractional shortening was more than 75 %. We can estimate the fractional shortening in the parasternal long axis view using M-mode by measuring the maximum ventricular dimension (end-diastolic dimension) and the minimum left ventricular dimension (end systolic dimension).

$$\text{Fractional shortening} = \frac{\text{EDD} - \text{ESD}}{\text{EDD}}$$

(EDD- Left ventricular end diastolic dimension, ESD- Left ventricular end systolic dimension)

High parasternal view: Using M mode the SVC diameter was measured. Maximum and minimum diameter at 6 different points were taken and then averaged which came as 0.21mm.

Low subcostal view: Using Pulsed wave mode, the SVC velocity time integral (VTI) was estimated as 9.39cm. Hear rate was 154m/s.
SVC flow was calculated as,

$$\text{SVC flow} = \frac{3.14 \text{ X } (\text{SVC Diameter})^2 \text{X SVC VTIX Heart Rate}}{4 \text{ X Weight}}$$

$$= 56.9 \text{ml/kg/min}$$

SVC flow was within normal limits (more than the operational threshold of 40 ml/kg/min (Kluckow and Evans, 2000). Hence we did not intervene and the mean blood pressure was subsequently more than 28mm Hg. Studies have shown that blood pressure weakly correlates with systemic blood flow (Osborn *et al*., 2004; Kluckow *et al*., 1996 and Pladys *et al*., 1999). In high flow states, due to low systemic vascular resistance (which is not directly measured) the blood pressure can be low with normal or high systemic blood flow. Similarly in neonates with high vascular resistance (when excessive vasopressors are used), blood pressure can be reassuringly high but the systemic blood flow can be pathologically low. During the trasitional period, due to increased blood flowing through the patent ductus arteriosus (ductal shunt) there is a falsely elevated left ventricular output (increased by up to 100%) and the blood flowing through a patent foramen ovale (atrial shunt) is reflected in a falsely elevated right ventricular output (Kluckow and Evans, 2001). Right ventricular output reasonably accurate marker of systemic blood flow compared to left ventricular output because large atrial shunt are not common (6%) in the initial 48 hours (Evans and Kluckow,

1996). Superior vena cava flow measurement, which is not affected by fetal shunts, have been validated as a reliable marker of systemic blood flow, and a reproducible normal range has been found in both term and preterm infants (Kluckow and Evans, 2000).

Case scenario III

A female term neonate, born at 38 weeks gestation, had meconium stained liquor was non-vigorous and required intratracheal suctioning. She was initially mechanically ventilated. Chest X-ray was suggestive of meconium aspiration syndrome. Echocardiography suggested severe pulmonary arterial hypertension (Fig. 3, Fig. 4).

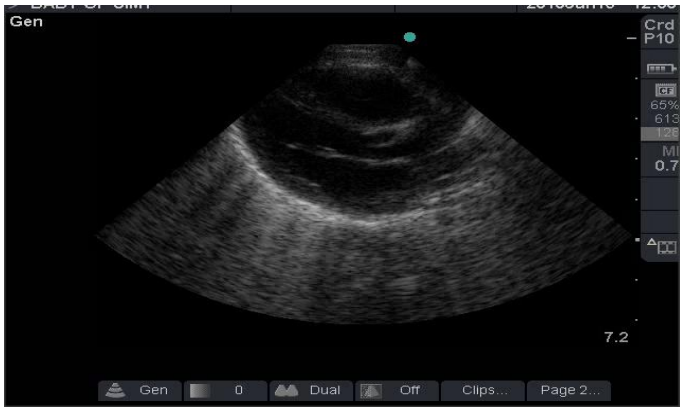

Fig.3. Parasternal long axis view: Globular dilated right ventricle with interventricular septum bend towards left ventricle

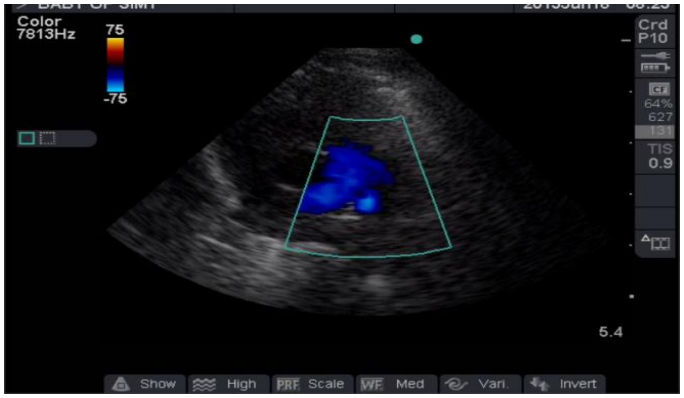

Fig.4. Parasternal short axis view: 3 legged stool sign showing right to left shunting though the ductus arteriosus indicated by the blue coloured third leg suggestive severe pulmonary hypertension

The neonate received sildenafil (Baquero *et al*., 2006) at 1 mg/kg/dose 6 hourly and milrinone (McNamara *et al*., 2006) at an infusion rate of 0.5 microgram/ka/min. Echocardiography done on the next day suggested persistence of the high pulmonary pressures. Sildenafil was increased to 2mg/kg/dose and Milrinone was gradually increased to 0.9 microgram/ kg/min. Gradually, the ventilator requirement came down and baby was extubated on day 6. Milrinone was tapered and stopped. Pulmonary pressures were serially monitored at 5 days interval and it was found to be normal on day 15, after which sildenafil was stopped. In the above described scenarios, clinical care was made better with Functional Echocardiography which supplements to the clinical assessment. The point of care use of echocardiography by the neonatologist can therefore give important information which would have been missed otherwise.

DISCUSSION

Neonatologists around the globe are acquiring skills to do functional echocardiography to supplement their clinical acumen. However it has to be emphasized that this tool is not to be used by the neonatologist to diagnose the structural heart disease. This tool has to be primarily used to detect problems in abnormal transition from fetal to neonatal circulation, which have been clearly elaborated in the above three case scenarios.

Functional echocardiography is used in the following situations (Skinner, 1998):

- Low systemic blood flow by estimating superior vena cava or right ventricular flow especially in transition period when the ductal steal will prevent the left ventricular output as a marker of systemic blood flow. To know the fluid status.
- Hemodynamic significant persistent ductus arteriosus.
- Persistent pulmonary hypertension of newborn.
- Miscellaneous: placement of central lines.

Reference to the Pediatric cardiologist is given in the following situations:

- Congenital heart disease is suspected.
- To rule out congenital heart disease in infants presenting with other congenital anomalies such as anorectal malformation, trachea-esophageal malformation, congential diaphragmatic hernia, choanal atresia.
- To rule out Ductus dependent critical congenital heart disease, especially when it is planned to treat the persistent ductus arteriosus.
- Functional echocardiography reveals previously unsuspected congenital heart disease.
- Routine screening echocardiogram

The dynamic course of hemodynamic status in term and preterm neonates (Kluckow and Evans, 2001 and Kluckow, 2005) demands 24 hour availability of a physician who knows to do echocardiography. The limited availability of the Pediatric Cardiologists prevents them to undertake this vital task. We receive a good supervisory support from our Pediatric cardiology division. Our Pediatric Cardiologists also does a routine echocardiography at 48 hours of life or earlier to rule out structural heart disease according to the clinical indications. Thus each neonatal unit, need some consultants if not all, with formal training in echocardiography. The need of the hour is to acknowledge functional echocardiography as a standard of practice in NICU and to devise educational programs and certification by relevant authorities. There should be support from the Government and the bureaucracy for the secure conduct of professional duties towards our neonatal patients. In summary, our experience supports the use of functional echocardiography as a routine practice in level 3

Neonatal units. It is an extension and not a replacement of clinical assessment of hemodynamic status of the patients. The apical authorities of Neonatology and Pediatric Cardiology need to formulate practice guidelines, curriculum for the training and certification. There should be mechanisms for the maintenance of competency through re-certification and continued medical education. There should be support from the local Pediatric Cardiologists who is in a good position to give the required guidance.

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Conflict of interest

None

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