Recent Topics in Fetal Cardiology

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ABSTRACT

The intraventricular pressure difference (IVPD) is the diastolic suction from the base to the apex during early diastole. This diastolic suction has been shown to actively contribute to rapid filling, which requires adequate filling under low pressure. The IVPD is an important cardiac diastolic functional marker in adults, children, and fetuses. Originally, IVPD could be measured only by direct hemodynamic monitoring; however, velocity estimation was made in the acquired color M-mode imaging, which was analyzed using originally developed programming. In this paper, IVPD analysis in normal fetuses as well as in cases of congenital heart disease has been shown. The IVPD is a useful tool for evaluating fetal diastolic function.

Keywords: Color M-mode, Diastolic function, Fetal cardiac function.

INTRODUCTION

Evaluation of fetal cardiac function is essential in many situations, such as twin-to-twin transfusion syndrome, fetal hydrops, intrauterine growth restriction, fetal arrhythmia, and congenital heart disease. There have been several ways to evaluate fetal cardiac function using the M-mode, Doppler flow, and tissue Doppler. In systolic functions, ejection fraction, cardiac output, and volumetric contraction time, and speckle tracking were used for evaluation. Isovolumetric relaxation time, E/A ratio, ejection time, E/e' with tissue Doppler are the parameters used to evaluate fetal diastolic function. The myocardial performance index (MPI) is a general marker used to evaluate fetal cardiac function. Fetal arterial and venous Doppler parameters are often used to evaluate the general fetal condition in obstetrics.¹² None of them is perfect for measuring fetal cardiac function.

The intraventricular pressure difference (IVPD) is the pressure difference from the basal to the apex of ventricle³ (Fig. 1). The IVPD is a diastolic suction force generated during early diastole, which is essential to induce an effective filling of the ventricle with low pressure.⁴ Theoretically, IVPD can be invasively measured with a catheter and occurs immediately after aortic valve closure in early diastole.³ Amount of IVPD is equal to the extent to which the ventricle can relax and relate to elastic recoil. It is important to determine whether this early ventricular filling is caused by the hemodynamic convective acceleration of blood during early diastole or caused by intracavitary volume redistribution with the dynamic shape change in the myocardium. In experiments using dogs that prevented ventricular diastolic filling with a remote-controlled mitral valve occluder, a negative pressure-volume relation was still seen in non-filling diastole, resulted in the independence of the hydrodynamics of blood inflow for the ventricular shape change. Eventually, the elastic recoil led to an intraventricular redistribution of chamber volume, local accelerations of blood, and associated intraventricular pressure gradients.⁶ Therefore, IVPD itself would be equal to diastolic function.

WHY IS INTRAVENTRICULAR PRESSURE DIFFERENCE USEFUL?

The IVPD in adults and children has been reported in previous reports. The IVPD is well correlated with the tau index, which is the gold standard of diastolic function and invasively measurable.⁷ In adults and children, during exercise, IVPD increased twice as much as at rest.⁵,⁸ Patients with cardiomyopathy showed a decreased IVPD.⁹ Increased IVPD correlated with peak VO₂max which was the strongest predictor of exercise capacity.¹⁰ Intraventricular pressure difference may play an important role in the measurement of diastolic function.

HOW TO MEASURE INTRAVENTRICULAR PRESSURE DIFFERENCE?

Initially, IVPD could be measured invasively using a catheter. The invasive method is not useful in clinical situations. In 2001, Greenberg et al. developed a system to calculate transmitral pressure differences across the mitral valve for the unsteady flow from the Bernoulli equation using a full digital velocity.¹¹ They explored the basic hydrodynamic principles to non-invasively obtained spatiotemporal velocity distribution of the left ventricular inflow.

Color Doppler with M-mode provides the spatiotemporal velocity distribution along an inflow streamline from the base to the apex. For fetal echocardiography, the apex position was determined according to the fetal position. If the apex is down, the color code is blue, and if the apex is up to the transducer,
the color code becomes red (Fig. 2). The brightness of the color display indicates the magnitude of the acceleration. The velocity distribution was extracted from the raw image file using our original program in MATLAB. After the early filling wave extraction, the pressure gradient was calculated using the one-dimensional Euler equation. The flow mapping in Figure 3 shows how to divide into velocity, time, and space, which leads to the pressure gradient (\(\frac{\partial P}{\partial s}\)) calculation. Based on the distance from the apex, segmental IVPDs (apical and mid-basal) were also measurable.

**Fig. 2:** Original color M-mode pictures to evaluate IVPD. The color bar was adjusted to red when the apex was directed toward the transducer. Meanwhile, the color bar was set to blue when the apex was lateral to the transducer

**Intraventricular Pressure Difference in Normal Fetuses**

In normal fetuses, the fetal myocardium is stiff and immature in the first- and mid-trimesters. It has pathological findings and different cardiac functional parameters. The fetal myocardium has less mitochondrial mass and less organized and different energy metabolism, which induces physiological myocardial stiffness. It acquires a greater diastolic function with maturation toward the term. We have shown that total IVPD at late gestation was
significantly greater than that at mid-gestation in both ventricles. Figure 4 shows the actual analysis in fetuses at 20 and 30 weeks of gestation. Interestingly, the percentage of apical IVPD increased at late gestation compared with that at mid-gestation; however, basal IVPD percentage decreased at late gestation. Since apical IVPD plays an important role in diastolic function, increased apical IVPD at late gestation makes sense to fetal physiology. Intraventricular pressure difference correlated well with stroke volume and cardiac output in both ventricles, which was consistent with the physiological mechanism of IVPD.

Figs 4A and B: IVPD with gestation in normal fetuses. (A) Acquired IVPD at 20 weeks of gestation; (B) Acquired IVPD at 30 weeks of gestation
In the case of pulmonary atresia with intact ventricular septum complicated by sinusoidal communications (Fig. 5A), impaired cardiac function induced fetal hydrops at 27 weeks of gestation. At the time of diagnosis of fetal hydrops, the obstructed cardiac lesion resulted in a wave reversal in the ductus venosus and umbilical venous pulsations. However, the cardiothoracic ratio (CTAR) was 0.45, tricuspid regurgitation (TR) = 405 cm/s, MPI = 0.38, total IVPD = 0.29 (mean for gestation = 0.37), mid-apical IVPD = 0.17 (Fig. 5B). At 28 weeks of gestation, CTAR = 0.53, TR = 354 cm/s, MPI = 0.46, total IVPD = 0.29 (mean for gestation = 0.39), mid-apical IVPD = 0.13. At 29 weeks of gestation, the cardiac function deteriorated as CTAR = 0.55, TR = 113 cm/s, MPI = 0.47, total IVPD = 0.19 (mean for gestation = 0.11), mid-apical IVPD = 0.04, which led to non-reassuring fetal status with fetal monitoring. Although cesarean section was performed to cure the baby, she was born at 1,112 g, umbilical artery pH = 7.30, and died soon after birth due to cardiac failure. Although it is necessary to verify these parameters under different conditions, the change in total and apical IVPD would be useful for evaluating fetal cardiac function.

**Conclusion**

The IVPD is a new useful marker for evaluating fetal cardiac diastolic function. Intraventricular pressure difference has a large potential to get around easily because of the simple way to collect the data with color M-mode.

**Acknowledgments**

We would like to thank Editage (www.editage.com) for English language editing.

**References**

1. Donofrio MT, Moon-Grady AJ, Hornberger LK, et al. Diagnosis and treatment of fetal cardiac disease: a scientific statement from the American Heart Association. Circulation 2014;129(21):2183–2242. DOI: 10.1161/01.cir.0000437597.44550.5d.

2. Rychik J, Tian Z, Bebbington M, et al. The twin-twin transfusion syndrome: spectrum of cardiovascular abnormality and development of a cardiovascular score to assess severity of disease. Am J Obstet Gynecol 2007;197(392):e1–e8. DOI: 10.1016/j.ajog.2007.06.055.

3. Courtois M, Kovacs SJ, Ludbrook PA. Transmitral pressure-flow velocity relation: Importance of regional pressure gradients in the left ventricle during diastole. Circulation 1988;78(3):661–671. DOI: 10.1161/01.cir.78.3.661.

4. Courtos M, Kovac SJ, Ludbrook PA. Physiological early diastolic intraventricular pressure gradient is lost during acute myocardial ischemia. Circulation 1990;81(5):1688–1696. DOI: 10.1161/01.cir.81.5.1688.

5. Notomi Y, Martin-Miklovic MG, Oryszak SJ, et al. Enhanced ventricular untwisting during exercise: a mechanistic manifestation of elastic recoil described by Doppler tissue imaging. Circulation 2006;113(21):2524–2533. DOI: 10.1161/CIRCULATIONAHA.105.596502.

6. Nikolic SD, Feneley MP, Pajaro OE, et al. Origin of regional pressure gradients in the left ventricle during early diastole. Am J Physiol 1995;268(2 Pt 2):550–557. DOI: 10.1152/ajpheart.1995.268.2.H550.
7. Steine K, Staugaard M, Smiseth OA. Mechanisms of diastolic intraventricular regional pressure differences and flow in the inflow and outflow tracts. J Am Coll Cardiol 2002;40(5):983–990. DOI: 10.1016/s0735-1097(02)02046-6.
8. Rovner A, Smith R, Greenberg NL, et al. Improvement in diastolic intraventricular pressure gradients in patients with HOCM after ethanol septal reduction. Am J Physiol Heart Circ Physiol 2003;285(6):2492–2499. DOI: 10.1152/ajpheart.00265.2003.
9. Yotti R, Bermejo J, Antoranz JC, et al. A noninvasive method for assessing impaired diastolic suction in patients with dilated cardiomyopathy. Circulation 2005;112(19):2921–2929. DOI: 10.1161/CIRCULATIONAHA.105.561340.
10. Rovner A, Greenberg NL, Thomas JD, et al. Relationship of diastolic intraventricular pressure gradients and aerobic capacity in patients with diastolic heart failure. Am J Physiol Heart Circ Physiol 2005;289(5):2081–2088. DOI: 10.1152/ajpheart.00951.2004.
11. Greenberg NL, Vandervoort PM, Firstenberg MS, et al. Estimation of diastolic intraventricular pressure gradients by Doppler M-mode echocardiography. Am J Physiol Heart Circ Physiol 2001;280(6):2507–2515. DOI: 10.1152/ajpheart.2001.280.6.H2507.
12. Pohjoismäki JLO, Krüger M, Al-Furoukh N, et al. Postnatal cardiomyocyte growth and mitochondrial reorganization cause multiple changes in the proteome of human cardiomyocytes. Mol Biosyst 2013;9(6):1210–1219. DOI: 10.1039/c3mb25556e.
13. Yamamoto Y, Takahashi K, Takemoto Y, et al. Evaluation of myocardial function according to early diastolic intraventricular pressure difference in fetuses. J Am Soc Echocardiogr 2017;30(11):1130–1137. DOI: 10.1016/j.echo.2017.07.013.