Perinatal Changes in Fetal Ventricular Geometry, Myocardial Performance, and Cardiac Function in Normal Term Pregnancies

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Background: The fetal heart at term is exposed to an increase in hemodynamic work as a consequence of fetal growth, increased circulating volume, and alteration in loading patterns due to maturational changes in fetoplacental circulation. The extent to which these cardiovascular changes influence human fetal and neonatal cardiac adaptation has not been fully elucidated. The aim of this study was to evaluate perinatal cardiovascular changes in ventricular geometry and myocardial performance in normal term fetuses.

Methods: Prospective study of 108 uncomplicated pregnancies delivering at term. M-mode, two-dimensional or B-mode, pulsed wave Doppler, pulsed wave tissue Doppler, and two-dimensional speckle tracking imaging were performed a few days before and within 24 hours of birth.

Results: Analysis of paired fetal and neonatal echoes demonstrated significant perinatal changes (P < .0001 for all) in right ventricular (RV) and left ventricular (LV) geometry (RV/LV end-diastolic dimension ratio, 1.2 vs 0.8; RV sphericity index, 0.53 vs 0.40; LV sphericity index, 0.46 vs 0.49). There were corresponding significant (P < .001 for all) perinatal changes in global myocardial performance: LV myocardial performance index, 0.60 versus 0.47; RV myocardial performance index, 0.61 versus 0.42; systolic function: LV longitudinal systolic strain rate, -1.4/sec versus -1.0/sec; RV longitudinal systolic strain rate, -1.5/sec versus -1.0/sec; RV sphericitic function: LV E'/A', 0.8 versus 1.1.

Conclusions: The findings support the concept that the perinatal period is associated with major changes in fetal ventricular geometry and cardiac function in response to significant alterations in loading conditions. Improved knowledge of perinatal cardiac changes in normal fetuses could facilitate better understanding of cardiac adaptation in normal and pathological pregnancies. (J Am Soc Echocardiogr 2017; \blacksquare : \blacksquare - \blacksquare .)

Keywords: Fetal echocardiography, Fetal heart, Myocardial performance index, Perinatal loading conditions, Speckle tracking, Tissue Doppler imaging

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INTRODUCTION

As the heart grows and develops in utero, it is exposed to an increase in hemodynamic work as a consequence of fetal growth, increased circulating volume, and alteration in loading patterns due to maturational changes in fetal and placental circulation. The developing heart may therefore be subject to considerable changes in ventricular geometry, myocardial performance, and cardiac function, especially at near term. The right ventricle is a dominant chamber in fetal life, supplying the lower body organs with less oxygenated blood through the ductus arteriosus.¹ The left ventricular (LV) output directs more oxygenated blood through the ascending aorta to the upper body, feeding the coronary and cerebral circulation. In this parallel fetal circulation, both ventricles are in communication with the descending aorta¹ and have similar systolic pressures but are still subject to different afterloads. Dramatic changes occur at birth with closure of the prenatal shunts, lowering of the pulmonary vascular resistance, increase in systemic vascular resistance, and the two ventricles now functioning in series. Although previous investigators have explored this phenomenon in animal models,² only few early³⁻⁶ and recent⁷⁻¹⁰ human

Abbreviations

- 2D = Two-dimensional
- AVV = Atrioventricular valve
- CO = Cardiac output
- CSA = Cross-sectional area
- ECG = Electrocardiogram
- **EDD** = End-diastolic dimension
- **ESD** = End-systolic dimension
- ET = Ejection time
- **fps** = Frames per second

ICC = Intraclass correlation coefficient

IVCT = Isovolumetric contraction time

IVRT = Isovolumetric relaxation time

IVS = Interventricular septal, septum

LoA = Limits of agreement

LV = Left ventricular

MPI = Myocardial performance index

PW = Pulsed wave

RT = Relaxation time

RV = Right ventricular

SF = Shortening fraction

STI = Speckle tracking imaging

SV = Stroke volume

- **TDI** = Tissue Doppler imaging
- **VTI** = Velocity time integral

studies have investigated the extent to which these cardiovascular changes influence the human perinatal cardiac adaptation, and they produced conflicting results.

A comprehensive assessment of the fetal heart at term may help to improve the understanding of perinatal fetal cardiac adaptation in normal and pathological pregnancies. Strain and strain rate analysis by tissue Doppler (TDI) and speckle tracking (STI) imaging has been found to have a stronger correlation to invasive indices of myocardial performance, a higher sensitivity for detecting even mild myocardial damage, and a stronger predictive value for cardiovascular complications than conventional echo indices.^{11,12} In spite of these newer techniques for cardiac imaging, there are few studies using these methods to assess perinatal fetal heart function in normal term pregnancies.⁸⁻¹⁰ The aim of this study was to characterize cardiac geometry and function in normal term fetuses and neonates and to describe how perinatal changes in loading conditions may have an impact on such parameters.

METHODS

This was a prospective longitudinal study involving the fetuses of women with apparently uncomplicated pregnancies and their newborn babies. Pregnant women attending for routine

antenatal care at St. George's Hospital between November 2012 and May 2014 were recruited if the pregnancies were assessed as normal and fetuses had structurally normal hearts. Exclusion criteria were fetal structural abnormality, impaired fetal growth, any maternal prepregnancy or pregnancy-related comorbidity, and pregnant women in labor. All participants gave written consent for fetal and neonatal echocardiogram. The Ethics Committee of NRES Committee London-Surrey Borders approved the study protocol (reference no. 12/LO/0945).

Fetal M-mode, two-dimensional (2D) or B-mode, spectral or pulsed wave (PW) Doppler, PW TDI, and STI echocardiograms were performed few days before birth. Neonatal cardiac assessment was conducted within hours after birth. One investigator (O.P.) performed all ultrasound examinations using a Toshiba Aplio MX ultrasound system (Toshiba Medical Systems, Japan). Fetal M-mode, B-mode, and PW Doppler measurements were made with the convex array transducer PVT-375BT (3.5 MHz), while the sector pediatric heart probe PST-65AT (6.5 MHz) was used for neonatal heart examination. Fetal and neonatal PW-TDI curves and 2D images for STI analysis were obtained and recorded with the multisector tissue harmonic transducer PST-30 BT (3 MHz) with TDI mode activated. All neonatal examinations were recorded with simultaneous electrocardiogram (ECG). In the absence of a fetal ECG, the cardiac cycle was determined from a dummy ECG device (Lionheart 2 BIO-TEK Multiparameter Simulator, BIO-TEK Instruments, Inc., Winooski, VT) and mechanical movements of the atrioventricular valves (AVVs).

M-mode ultrasound was used for assessment of LV shortening fraction (SF) and longitudinal axis ventricular systolic function. B-mode (2D) imaging was performed to measure ventricular chambers (right ventricular [RV] and LV end-diastolic dimensions [EDDs], end-systolic dimensions [ESDs], RV/LV EDD ratio, ventricular end-diastolic and end-systolic areas, and RV and LV sphericity index calculated by dividing ventricular EDD by ventricular end-diastolic length in the apical/basal four-chamber view), ventricular wall thickness, and valve diameters. The PW Doppler technique was used to obtain Doppler signals from the inflow and outflow tracts for evaluation of diastolic and systolic function, respectively, for calculation of stroke volume (SV) and cardiac output (CO) and for estimation of LV myocardial performance index (MPI). The PW-TDI technique was applied to derive cardiac indices of myocardial motion S' as well as E' and A' and was also used for estimation of MPI for both right and left ventricles (MPI'). All echocardiographic measurements were performed according to the standardized protocol of the study and with regards to previously described fetal echo techniques (see the Supplemental Data, available at www.onlinejase.com). For fetal STI, care was taken to obtain 2D four-chamber apical or basal images. The narrowest possible ultrasound field and a single focal zone were used during image acquisition to obtain the frame rates greater than 100 frames per second (fps). These settings provided an acceptable combination of high temporal resolution with spatial definition to enhance the feasibility of the frame-by-frame tracking technique. Following the observation of several fetal heart beats, the real-time image was frozen, and one cardiac cycle was recorded. With the dummy ECG set at 60 bpm, the system was able to capture at least one whole fetal cardiac cycle with real fetal heart rate of 120-150 bpm. When several digital clips were obtained, raw data were transferred to a computer for offline analysis with frame rates greater than 100 fps using a dedicated software (TDI and STI Toshiba software Advanced Cardiac Package, Toshiba Medical Systems, Japan) on a BTO laptop. The 2D clips were visually inspected, and the one with the best endocardial border definition was chosen for STI analysis. The cardiac cycle was defined with M-mode function (M-Graph) incorporated into the Toshiba software whereby an M-mode trace was obtained by placing a cursor line on the 2D image. This provided a guide to set the R wave position. Visualization of opening (start of the diastole) and closure (start of systole) of AVVs was used to confirm definition of the cardiac cycle. The endocardial and epicardial surfaces of the myocardial segment were manually traced by a point-and-click approach. When the trace was recognized and accepted by the software, it was then automatically generated by the system by creating a region of interest and providing segmental longitudinal strain and strain rate values and then generated strain and strain rate curves for each selected myocardial segment. From these curves, the regional and global (by averaging values observed in all six segments) peak values were obtained. The peak systolic values of global and segmental longitudinal strain and systolic longitudinal strain rate were recorded for LV and RV separately. All temporal indices (PW-TDI derived time intervals) were

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