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The Impact of Maternal Gestational Hypertension and the Use of Anti-Hypertensives on Neonatal Myocardial Performance

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Neonatal myocardial performance · Maternal gestational hypertension · Ventricular function

Abstract
Background: Assessment of myocardial performance in neonates using advanced techniques such as deformation imaging and rotational mechanics has gained considerable interest. The applicability of these techniques for elucidating abnormal myocardial performance in various clinical scenarios is becoming established. We hypothesise that term infants born to mothers with gestational hypertension (GH) may experience impaired performance of the left and right ventricles during the early neonatal period. ***Objectives:*** We aimed to assess left and right ventricular (LV and RV) function using echocardiography in infants born to mothers with GH and compare them to a control group. ***Methods:*** Term infants (>36^{+6} weeks) born to mothers with GH underwent assessment to measure biventricular function using ejection fraction (EF), deformation imaging, left-ventricle rotational mechanics (apical rotation, basal rotation, twist, twist rate, and untwist rate), and right ventricle-specific functional parameters (tricuspid annular plane systolic excursion and fractional area change) in the first 48 h after birth. A control group comprising infants born to healthy mothers was used for comparison. ***Results:*** Fifteen infants with maternal GH and 30 age-matched controls were enrolled. The GH infants exhibited no differences in birthweight or LV or RV length, but they had lower EF (54 vs. 61%; $p < 0.01$), LV global longitudinal strain (–20 vs. –25%; $p < 0.01$), and LV twist (11 vs. 16°; $p = 0.04$). There were no differences in any of the RV functional parameters. ***Conclusion:*** Infants born to mothers with GH exhibited lower LV function than healthy controls, while RV function appeared to be preserved. This relationship warrants further exploration in a larger cohort.

Introduction

Abnormalities in utero-placental function during pregnancy result in maternal and foetal complications including pre-eclampsia (PE), gestational hypertension

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(GH), and intra-uterine growth restriction (IUGR). These pathological processes increase neonatal morbidity and mortality as they frequently lead to delivery at preterm gestations. In addition, an abnormal intra-uterine environment can have a direct effect on the cardiovascular well-being of infants in the immediate post-natal period [1]. Maternal PE results in increased natriuretic peptide and homocysteine in neonates (suggesting abnormal myocardial function) [2], and children born to mothers with PE have altered cardiac profiles compared with controls when assessed using echocardiography at 5–8 years of age [3]. In addition, IUGR infants demonstrate altered cardiac morphology and reduced myocardial function in the first week of life [4]. In addition, small for gestational age (SGA) infants have subtle alterations in left and right myocardial function during the early neonatal period [5], which remains evident on echocardiography in the first 6 months of age [6].

Studies on the effect of GH and maternal anti-hypertensive drug therapy on myocardial performance in appropriately grown neonates during the immediate post-natal period are lacking, however. Drugs commonly used to treat GH include labetalol and nifedipine. Beta-receptor and calcium-channel blockade in the mother may have an impact on cardiac performance in the neonate, and studies have demonstrated neonatal effects of antenatal labetalol exposure including hypoglycaemia, bradycardia, and altered cerebral auto-regulation [7, 8]. With the emergence of new echocardiography modalities including the deformation and rotational characteristics of the left ventricle, and right ventricle-specific measurements, a detailed characterisation of myocardial performance in various disease states and physiological milieus is now possible [9, 10]. Those measurements are feasible in the neonatal population and demonstrate excellent intra- and inter-rater reproducibility [11, 12].

In this study, we hypothesised that infants born to mothers with GH treated with labetalol would have reduced left and right ventricular (LV and RV) function when compared with healthy controls. We performed a cross-sectional study using novel echocardiography techniques, with the aim of comparing the cardiac performance of this hypertensive group with a control group.

Methods

This was a prospective observational cross-sectional study of infants born in the Rotunda Hospital, Dublin, Ireland, a tertiary maternity hospital with >8,500 deliveries per annum. Infants born with a gestational age of $>36^{+6}$ weeks were eligible and were recruited from the Haemodynamic Assessment in Pregnancy and Neonatal Echocardiography (HANDLE) study. Ethical approval was obtained from the hospital's research ethics board and written informed consent was obtained from all parents prior to enrollment. We enrolled infants born to mothers with gestational hypertension (GH), defined as maternal blood pressure of ≥140/90 on 2 occasions during pregnancy and requiring treatment; these mothers were all normotensive at the time of booking to hospital. We excluded mothers who had subsequently developed diabetes, PE, clinical chorioamnionitis, or absent/reversed end-diastolic flow in the umbilical arteries at any time during pregnancy. In addition to this, we enrolled a cohort of normal, healthy, appropriately grown infants (in a 2:1 ratio) at term, born to mothers with no illness or medication use during pregnancy. Only singleton pregnancies were considered. The short-term clinical outcomes of the recruited infants, including NICU admission, hypoglycaemia, and transient tachypnoea of the newborn were recorded. We also recorded maternal demographics including age, weight, and body mass index (BMI), and neonatal data including gestation, birthweight, mode of delivery, 5-min Apgar score, and cord pH.

Echocardiography

A single echocardiogram was performed for infants in both groups within the first 48 h following birth using a Vivid S6 echocardiography machine (General Electric, Milwaukee, WI, USA) by a single operator (C.R.B.). Images were acquired using a 7-MHz probe, and optimised to visualise the myocardial walls [13]. All infants were haemodynamically stable at the time of scanning and placed in a supine position [14]. The echocardiography images and cine loops were stored as raw data and analysed later using dedicated vendor-customised commercially available software (EchoPAC v112; General Electric Medical Systems, Waukesha, WI, USA). A comprehensive echocardiographic assessment to measure bi-ventricular function was performed; detailed methodology is described elsewhere [11, 12, 15].

Ejection fraction (EF) was measured using the Simpson's Biplane method, and LV dimensions including length in diastole, mitral valve (MV) annular diameter and LV end-diastolic diameter (LVEDD). Left atrial/aortic root ratio (LA:Ao), MV E, MV A and MV velocity time index were also measured as surrogates of LV preload. Deformation imaging (LV and RV systolic longitudinal strain and systolic strain rate) was measured using validated image acquisition and analysis protocols [13, 16–18]. Left-ventricle rotational mechanics (apical rotation, basal rotation, twist, twist rate, and untwist rate) were obtained. We recorded clockwise rotation as negative, and anti-clockwise rotation as positive. The value for twist was the net effect of the apical and basal rotation using the following formula: twist (°) = apical rotation (°) – basal rotation (°). Torsion is the value assigned when LV twist is indexed to LV length in the end diastole using the following formula: torsion (°/cm) = LV twist (°)/LV length (cm). LV twist rate (LVTR) is the speed at which the LV twists (°/s) in the systole, and LV untwist rate (LVUTR) is the speed at which the LV untwists (°/s) in early diastole.

The RV annulus and mid-cavity diameters as well as RV length were obtained from an RV-focused 4-chamber view at end diastole. Tricuspid annular plane systolic excursion was measured from the apical 4-chamber view using the M-mode [19]. Fractional area change was measured from the RV 4-chamber view [20].

Table 1. Maternal characteristics and infant birth demographics

	GH group (n = 15)	Controls (n = 30)	p value
Maternal age, years	32 (30–35)	29 (25–32)	0.03
Maternal weight, kg	71 (61–81)	63 (58–78)	0.61
Maternal BMI	26 (24–28)	24 (22–28)	0.30
Blood pressure at admission[a]			
Systolic, mm Hg	128 (115–133)	125 (113–129)	0.06
Diastolic, mm Hg	73 (68–85)	69 (66–76)	0.07
Ethnicity			
Caucasian	13 (87)	27 (90)	0.82
African	0 (0)	7 (7)	
Asian	2 (13)	1 (3)	
Smoker	0 (0)	6 (20)	0.16
Gestational age, weeks	39.4 (38.8–40.5)	40.0 (39.7–41.1)	0.19
Birthweight, g	3,390 (2,910–3,560)	3,515 (3,210–3,900)	0.21
Male	7 (47)	18 (60)	0.53
Caesarean section	8 (53)	4 (13)	0.01
5-min Apgar score	10	10	0.78
Cord pH	7.31 (7.26–7.35)	7.29 (7.26–7.33)	0.81
Neonatal hypoglycaemia	3 (20)	0	0.03

Data are presented as median (inter-quartile range) or n (%).
[a] Between 14 and 16 weeks' gestation.

Statistical Analysis

Continuous data were presented as mean (standard deviation), compared using the independent Student t test, or median (inter-quartile range), compared using the Mann-Whitney U test. Categorical variables were presented as n (%) and compared using the χ^2 test (or the Fisher exact test as appropriate). Correlations were tested using the Pearson correlation coefficient. Multi-variate linear regression was used to test the independent association between important variables and functional parameters. A p value <0.05 was considered significant. SPSS (v23, IBM) was used to conduct the statistical analysis.

Results

Forty-five infants were enrolled in the study: 15 born to mothers with GH and 30 controls. Table 1 illustrates the maternal and infant characteristics in the 2 groups. Mothers with GH were slightly older than controls but had a similar weight, BMI, ethnic origin, and smoking status. Infants born to mothers with GH were similar to those born to healthy mothers, with no differences in gestation, birthweight, 5-min Apgar score, or cord pH. There was a higher rate of caesarean section in the GH group. There were no differences in systolic or diastolic blood pressure between the 2 groups at admission. All mothers in the GH group were in receipt of labetalol and 1 was receiving additional nifedipine at the time of delivery. Echocardiography was performed at a median of 27 h (17–44 h) after delivery.

Infants born to mothers with GH had a lower incidence of patent ductus arteriosus (PDA) at the time of the scan (Table 2). There was no difference in LA:Ao or LVEDD between the 2 groups, and no difference in LV dimensions. Infants in the GH group had a lower mean EF: 54% (6) versus 61% (6) (p < 0.01); lower mean LV global longitudinal strain (GLS): –20% (2) versus –25% (3) (p < 0.01); and a lower LV twist: 11° (8) versus 16° (6) (p = 0.04). Strain rate, basal rotation, twist rate, and untwist rate were similar in the 2 groups. There were no differences in any of the RV functional or dimensional measurements between the 2 groups.

The effect of potential confounding variables (maternal age, infant birthweight, mode of delivery, and PDA) on functional parameters was examined in a linear regression. Group assignment (GH vs. control) remained independently associated with EF and LV GLS but not with LV twist; this became a trend (Table 3).

Table 2. Myocardial function

	GH group (n = 15)	Controls (n = 30)	p value
Median (IQR) time of scan after birth, h	27 (22–34)	27 (14–42)	0.94
Heart rate, bpm	128 (9)	119 (15)	0.07
PDA and preload surrogates			
PDA, n (%)	1 (7)	9 (31)	0.13
PDA diameter, mm	2.8	2.0 (0.6)	0.22
LA:Ao	1.4 (0.3)	1.2 (0.1)	0.1
Mitral inflow E:A ratio	1.1 (0.2)	1.1 (0.2)	0.98
Mitral inflow VTI	8.4 (1.2)	8.3 (1.9)	0.94
LV dimensions			
MV annular diameter, mm	9.5 (1.3)	9.4 (1.1)	0.77
LVEDD, mm	18 (2)	18 (2)	0.39
Septal wall thickness, mm	2.7 (0.5)	2.6 (0.4)	0.41
LV posterior wall thickness, mm	2.2 (0.6)	2.3 (0.6)	0.53
LV length, mm	27 (2)	28 (2)	0.28
LV function			
Ejection fraction, %	54 (6)	61 (6)	<0.01
Global longitudinal strain, %	−20 (2)	−25 (3)	<0.01
Global longitudinal systolic SR, 1/s	−1.9 (0.4)	−2.0 (0.3)	0.25
Apical rotation	15° (5°)	17° (5°)	0.31
Basal rotation	4° (8°)	0.9° (4.3°)	0.25
Twist	11° (8°)	16° (6°)	0.04
Twist rate, °/s	145 (58)	151 (47)	0.74
Untwist rate, °/s	−170 (84)	−188 (53)	0.43
RV function and dimensions			
RV length, mm	26 (3)	27 (2)	0.44
TV annular diameter, mm	9.7 (1.5)	9.9 (1.4)	0.55
RV mid-cavity diameter, mm	12.6 (1.9)	12.9 (1.4)	0.54
TAPSE, mm	8.7 (1.7)	8.4 (1.1)	0.57
RV fractional area change, %	26 (7)	25 (4)	0.18
RV longitudinal strain, %	−23 (4)	−25 (4)	0.18
RV longitudinal SR, 1/s	−2.0 (0.8)	−2.3 (0.8)	0.30

Values are presented as mean (SD), unless otherwise indicated. PDA, patent ductus arteriosus; LA:Ao, left atrial/aortic root ratio; VTI, velocity time integral; MV, mitral valve; LVEDD, left ventricular end-diastolic diameter; LV, left ventricular; SR, strain rate; RV, right ventricular; TV, tricuspid valve; TAPSE, tricuspid annular plain systolic excursion.

Discussion

In this study, we demonstrated that infants born to mothers with GH and treated with labetalol exhibited lower LV function, illustrated by lower EF, LV GLS, and LV twist values. These differences remained significant following adjustment for maternal age, infant birthweight, and mode of delivery. There was preservation of RV function with no differences in any of the RV functional parameters.

Previous research has primarily focused on the assessment of infants born to mothers with overt evidence of utero-placental disease such as PE and IUGR, and demonstrated reduced LV diastolic function in premature infants born to mothers with PE in the first week after delivery [21]. The presence of this dysfunction is further supported by the finding of an elevation in the levels of certain cardiac enzymes at birth [2]. In addition, infants born SGA exhibit significantly reduced LV GLS (−15.9 vs. −21.3%) compared to appropriately grown infants during the early neonatal period, and this has been related to the degree of arterial stiffness [22]. Other studies have demonstrated that myocardial dysfunction in SGA infants involves both ventricles in systole and diastole [5]. This car-

Table 3. Association between group allocation (maternal GH vs. control) and functional measurements adjusting for maternal age, infant birthweight, mode of delivery, and patent ductus arteriosus

Dependent variable	Group assignment[a]	*p* value
Global longitudinal strain	0.42	0.02
Ejection fraction	0.54	0.003
LV twist	0.37	0.09

[a] Standardised β coefficient.

diac dysfunction may represent the effects of both uteroplacental insufficiency and prematurity. Adverse loading conditions experienced by the myocardium of SGA infants which manifests due to increased aortic stenosis also contribute to dysfunction. In our study, all infants (in the GH and control arms), were born at term and were of normal birthweight. In the absence of evidence of uteroplacental disease, it is therefore likely that any differences in function identified in our study are due to drug exposure.

Our study utilised novel markers which more accurately reflect cardiac performance. Normative values for GLS are becoming established in neonatology and form a basis for comparison with disease states. The values obtained in our normal infants are similar to those obtained in other studies by our group and are in keeping with a recent systematic review of normative deformation values in children and neonates [23]. Variations in reference ranges between different normal populations could be explained by the timing of the scans, the type and version of software used for measurements, and the measurement techniques [24].

We found a reduction in LV function measures using EF and deformation in infants born to mothers with GH who were in receipt of labetalol. In addition, net LV twist was reduced in this group of infants. Such measurements are influenced by a combination of loading conditions in addition to inherent contractility. The relative lack of difference in load-independent parameters (strain rate, twist rate, and untwist rate) suggest that neonatal loading conditions are altered by labetalol exposure [25]. None of the surrogates of preload measurements (LA:Ao, LVEDD, MV E:A, and MV velocity time integral) differed between the 2 groups, and the observed relationship between GH/labetalol use and the function measurement remained significant when controlling for PDA. Therefore, the β-receptor blocker effect cannot be completely discounted as a contributor to the reduced function. RV function is less impacted by β blockade and this may explain the lack of difference in RV performance between the 2 groups. We can speculate that maternal GH and/or labetalol treatment may induce subtle LV-specific morphological changes. This relationship warrants further exploration in a larger cohort.

This study was limited by the small number of infants, as more subtle differences between the groups may not have been identified as significant. The neonatal echocardiograms were carried out at only 1 time point, so we cannot comment on changes to cardiac performance over time. It would have been interesting to assess the changes in functional parameters when labetalol had been cleared. The rate of clinical events in both groups was low and we did not measure blood pressure; as such, we could not assess the relationship between myocardial function and clinical outcomes.

Conclusion

With the use of novel echocardiography techniques, we found evidence of LV dysfunction in infants born to mothers receiving anti-hypertensive therapy for gestational hypertension compared to healthy controls. RV function appeared to be spared. Further research is warranted to explore the impact of an abnormal in utero haemodynamic environment and exposure to cardiotropic medication on both foetal and neonatal myocardial performance, to confirm this association with a larger cohort, and to evaluate the potential long-term implications.

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Disclosure Statement

The authors have nothing to disclose.

References

1 Barker DJ, Winter PD, Osmond C, Margetts B, Simmonds SJ: Weight in infancy and death from ischaemic heart disease. Lancet 1989;2:577–580.

2 Akil A, Api O, Oten Can E, Ozkan S, Ercan S, Orcun A, Unal O: Does preeclampsia have any adverse effect on fetal heart? J Matern Fetal Neonatal Med 2016;29:2312–2315.

3 Fugelseth D, Ramstad HB, Kvehaugen AS, Nestaas E, Stoylen A, Staff AC: Myocardial function in offspring 5–8 years after pregnancy complicated by preeclampsia. Early Hum Dev 2011;87:531–535.

4 Fouzas S, Karatza AA, Davlouros PA, Chrysis D, Alexopoulos D, Mantagos S, Dimitriou G: Neonatal cardiac dysfunction in intrauterine growth restriction. Pediatr Res 2014;75:651–657.

5 Faienza MF, Brunetti G, Delvecchio M, Zito A, De Palma F, Cortese F, Nitti A, Massari E, Gesualdo M, Ricci G, Carbonara S, Giordano P, Cavallo L, Scicchitano P, Ciccone MM: Vascular function and myocardial performance indices in children born small for gestational age. Circ J 2016;80:958–963.

6 Altin H, Karaarslan S, Karatas Z, Alp H, Sap F, Baysal T: Evaluation of cardiac functions in term small for gestational age newborns with mild growth retardation: a serial conventional and tissue Doppler imaging echocardiographic study. Early Hum Dev 2012;88:757–764.

7 Caicedo A, Varon C, Thewissen L, Naulaers G, Lemmers P, Van Bel F, Van Huffel S: Influence of the maternal use of labetalol on the neurogenic mechanism for cerebral autoregulation assessed by means of NIRS. Adv Exp Med Biol 2014;812:173–179.

8 Bateman BT, Patorno E, Desai RJ, Seely EW, Mogun H, Maeda A, Fischer MA, Hernandez-Diaz S, Huybrechts KF: Late pregnancy β blocker exposure and risks of neonatal hypoglycemia and bradycardia. Pediatrics 2016;138:e20160731.

9 El-Khuffash AF, Jain A, Weisz D, Mertens L, McNamara PJ: Assessment and treatment of post patent ductus arteriosus ligation syndrome. J Pediatr 2014;165:46–52.

10 James AT, Corcoran JD, Hayes B, Franklin O, El-Khuffash A: The effect of antenatal magnesium sulfate on left ventricular afterload and myocardial function measured using deformation and rotational mechanics imaging. J Perinatol 2015;35:913–918.

11 Jain A, El-Khuffash AF, Kuipers BC, Mohamed A, Connelly KA, McNamara PJ, Jankov RP, Mertens L: Left ventricular function in healthy term neonates during the transitional period. J Pediatr 2017;182:197–203.

12 Jain A, Mohamed A, El-Khuffash A, Connelly KA, Dallaire F, Jankov RP, McNamara PJ, Mertens L: A comprehensive echocardiographic protocol for assessing neonatal right ventricular dimensions and function in the transitional period: normative data and *z* scores. J Am Soc Echocardiogr 2014;27:1293–1304.

13 Levy PT, Holland MR, Sekarski TJ, Hamvas A, Singh GK: Feasibility and reproducibility of systolic right ventricular strain measurement by speckle-tracking echocardiography in premature infants. J Am Soc Echocardiogr 2013;26:1201–1213.

14 Mertens L, Seri I, Marek J, Arlettaz R, Barker P, McNamara P, Moon-Grady AJ, Coon PD, Noori S, Simpson J, Lai WW; Writing Group of the American Society of Echocardiography; European Association of Echocardiography; Association for European Pediatric Cardiologists: Targeted neonatal echocardiography in the neonatal intensive care unit: practice guidelines and recommendations for training. J Am Soc Echocardiogr 2011;24:1057–1078.

15 Breatnach CR, Forman E, Foran A, Monteith C, McSweeney L, Malone F, McCallion N, Franklin O, El-Khuffash A: Left ventricular rotational mechanics in infants with hypoxic ischemic encephalopathy and preterm infants at 36 weeks postmenstrual age: a comparison with healthy term controls. Echocardiography 2017;34:232–239.

16 El-Khuffash AF, Jain A, Dragulescu A, McNamara PJ, Mertens L: Acute changes in myocardial systolic function in preterm infants undergoing patent ductus arteriosus ligation: a tissue Doppler and myocardial deformation study. J Am Soc Echocardiogr 2012;25:1058–1067.

17 Sanchez AA, Levy PT, Sekarski TJ, Hamvas A, Holland MR, Singh GK: Effects of frame rate on two-dimensional speckle tracking-derived measurements of myocardial deformation in premature infants. Echocardiography 2015;32:839–847.

18 James A, Corcoran JD, Mertens L, Franklin O, El-Khuffash A: Left ventricular rotational mechanics in preterm infants less than 29 weeks' gestation over the first week after birth. J Am Soc Echocardiogr 2015;28:808–817.

19 Koestenberger M, Nagel B, Ravekes W, Urlesberger B, Raith W, Avian A, Halb V, Cvirn G, Fritsch P, Gamillscheg A: Systolic right ventricular function in preterm and term neonates: reference values of the tricuspid annular plane systolic excursion (TAPSE) in 258 patients and calculation of Z-score values. Neonatology 2011;100:85–92.

20 Levy PT, Dioneda B, Holland MR, Sekarski TJ, Lee CK, Mathur A, Cade WT, Cahill AG, Hamvas A, Singh GK: Right ventricular function in preterm and term neonates: reference values for right ventricle areas and fractional area of change. J Am Soc Echocardiogr 2015;28:559–569.

21 Cetinkaya M, Bostan O, Koksal N, Semizel E, Ozkan H, Cakir S: Early left ventricular diastolic dysfunction in premature infants born to preeclamptic mothers. J Perinat Med 2011;39:89–95.

22 Sehgal A, Doctor T, Menahem S: Cardiac function and arterial indices in infants born small for gestational age: analysis by speckle tracking. Acta Paediatr 2014;103:e49–e54.

23 Levy PT, Machefsky A, Sanchez AA, Patel MD, Rogal S, Fowler S, Yaeger L, Hardi A, Holland MR, Hamvas A, Singh GK: Reference ranges of left ventricular strain measures by two-dimensional speckle-tracking echocardiography in children: a systematic review and meta-analysis. J Am Soc Echocardiogr 2016;29:209–225 e206.

24 Breatnach CR, Levy PT, James AT, Franklin O, El-Khuffash A: Novel echocardiography methods in the functional assessment of the newborn heart. Neonatology 2016;110:248–260.

25 Ferferieva V, Van den Bergh A, Claus P, Jasaityte R, Veulemans P, Pellens M, La GA, Rademakers F, Herijgers P, D'hooge J: The relative value of strain and strain rate for defining intrinsic myocardial function. Am J Physiol Heart Circ Physiol 2012;302:H188–H195.