

**PRETERM CARDIAC DEVELOPMENT: FETAL AND NEONATAL
ECHOCARDIOGRAPHY REVEALS THAT DIFFERENCES IN CARDIAC
VENTRICULAR MASS AND FUNCTION DEVELOP IN EARLY POSTNATAL
LIFE**

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ABSTRACT

Background- Offspring born preterm (<37 weeks gestation) have increased left and right ventricular mass, smaller internal cavity dimensions and reduced systolic and diastolic function in young adulthood. We hypothesized that this distinct cardiac phenotype would begin to develop in early postnatal life as a result of the premature exposure of the immature heart to the physiological stresses of the ex utero environment.

Purpose— We sought to determine whether differences between preterm- and term-born individuals in right and left ventricular structure and function occur during fetal life or whether they emerge during early postnatal life.

Methods- 255 infants born either preterm or term were recruited for cardiac imaging using echocardiography at birth and three months of age in order to perform cardiac phenotyping (structure and function). We also recruited 189 fetuses for fetal echocardiography between 15 and 42 weeks gestation in order to study structural cardiac development *in utero* in preterm and term pregnancies.

Results- The preterm group had a proportionally similar cardiac structure compared to term offspring at birth, with similar cardiac growth trajectories during fetal life. By three months of age, preterm-born neonates had a significantly increased mass/end-diastolic volumes ratio in both the left and right ventricle (left $p=0.005$, right $p=0.04$) with a percentage mass change indexed to body surface area in the preterm group more than double compared to controls in the left and right ventricle (left 57.8 ± 41.9 vs 27.3 ± 29.4 %, $p<0.001$; right 39.3 ± 38.1 vs 16.6 ± 40.8 %, $p=0.002$). The percentage mass index change was significantly correlated with gestational age at birth in both ventricles (left $r= -0.49$ $p<0.001$; right $r=-0.37$ $p=0.001$) and increase in mass in the postnatal period was over and above what would have been expected for their postnatal age. The preterm group also demonstrated reduced left ventricular diastolic function with a significantly increased lateral E/E' ratio at three months of age which was significantly correlated with left ventricular mass change ($r=0.21$ $p=0.01$).

Conclusions- Offspring born preterm and term have a similar cardiac development *in utero* but, post birth, have a disproportionate increase in left and right ventricular mass over the first three months of life, which is associated with reduced left ventricular diastolic function. These findings suggest that early postnatal life is a critical period of altered cardiac development in preterm-born infants. Whether these cardiac changes are modifiable in the short and long term will be of future interest in order to reduce cardiovascular risk in this growing subgroup of the population.