Impact of prenatal life on cardiovascular long term health

Challenges and opportunities for (predictive) fetal medicine

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Biological programming and age

IMPACT OF ENVIRONMENT

Fetal Programming

epigenetics

Fetus

Child

TIME

How the first nine months shape the rest of your life

The new science of fetal origins

BY ANNE MURPHY PAUL
1986 Barker (MRC Unit, Southampton, UK):
Coronary heart disease mortality rates

Death rates from Coronary Heart Disease in men 1968-79 vs Mortality 1901-1910

FETAL CARDIOVASCULAR PROGRAMMING

LOW BIRTHWEIGHT

placental insufficiency

fetal cardiac dysfunction

CARDIOVASCULAR DISEASE IN ADULTHOOD

hypertension

coronary disease

stroke

obesity

diabetes

fetal cardiovascular remodeling

PLACENTAL INSUFFICIENCY COMPENSATED HYPOXIA

DECOMPENSATED HYPOXIA INJURY - DEATH

brain vasodilation

↓longitudinal motion impaired relaxation

more globular heart
less oxygen consumption
increased wall stress
maintained cardiac output

Crispi AJOG 2008, Comas UOG 2011, Cruz UOG 2013
INTRAUTERINE GROWTH RESTRICTION

fetal cardiac dysfunction

postnatal persistance of cardiovascular remodeling

hypertension coronary disease stroke obesity diabetes

cardiovascular disease in adulthood

postnatal cardiovascular remodelling

Cardiovascular remodelling

- globular heart
- ↓ longitudinal motion
- ↓ stroke volume
- ↑ heart rate
- = cardiac output

hypertension
pre-arteriosclerosis

TA 90/65
clMT = 0.386 mm

TA 115/80
clMT = 0.434 mm

IMPACT OF LATE IUGR/SGA

near term SGA fetuses without signs of poor prognosis also presented CV remodeling

ASSISTED REPRODUCTIVE TECHNOLOGIES

- embryo manipulation
- epigenetic changes

FETAL CARDIOVASCULAR PROGRAMMING

worse perinatal outcomes

systemic & pulmonary vascular dysfunction

- control: n=100
- ART: n=100

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<tr>
<th></th>
<th>controls</th>
<th>ART</th>
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<tbody>
<tr>
<td>Right atrial area (cm²)</td>
<td>1.46 (1.2-1.5)</td>
<td>1.60 (1.3-1.8)*</td>
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<tr>
<td>Right sphericity index</td>
<td>1.58 (1.4-1.72)</td>
<td>1.37 (1.25-1.5)*</td>
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<tr>
<td>Septal wall thickness (mm)</td>
<td>2.4 (2.4-2.8)</td>
<td>2.7 (2.4-2.9)*</td>
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*P<0.05 adjusted by gestational age at delivery, birth weight centile and preeclampsia
ART= fetuses conceived by assisted reproductive technologies.
decreased systolic motion  impaired relaxation

data are median + SEM. *P<0.05 adjusted by GA, birthweight centile and preeclampsia.
Fetal cardiovascular programming of adult disease

- Intrauterine growth restriction
- Assisted reproductive technologies
- Maternal diabetes
Impact of environment on CV programming through the window of opportunity for correction.

- Placental disease
- ART
- Diabetes
- HAART
- Infection

Opportunity for correction between the fetus and child stages can mitigate CV programming leading to disease in later life.
IDENTIFICATION OF RISK

INDIVIDUAL BIOMARKERS

INTERVENTION

WINDOW OF OPPORTUNITY

BIRTH

Fetus

Problem evident

Child

Functional / structural organ remodeling

4P medicine

- Predictive
- Preventive
- Personalized
- Participatory

fetal composite CV score for the prediction of postnatal hypertension
sensitivity 90%, specificity 77%

Cruz-Lemini FMF 2013, Skilton Pediatric 2012, Rodriguez 2013
• Environmental insults *in utero* have an impact on cardiovascular long-term adult health

• Fetal echocardiography allows the prediction of postnatal hypertension and arterial remodeling, identifying a high-risk group, which could be targeted for promoting healthy diet and physical exercise.

• Early detection and intervention of cardiac remodeling may improve future cardiovascular health in fetuses from high-risk pregnancies

thank you
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