The Future of Fetal Cardiology

Da Vinci 1510

Edgar Jaeggi, MD, FRCPC  www.sickkids.ca/FetalCardiacProgram
Objectives

Discuss some of the recent developments in fetal cardiology

- Trends in prenatal detection
- Emerging imaging tools
- Prenatal therapy
Identification of congenital cardiac malformations by echocardiography in midtrimester fetus*

LINDSEY D ALLAN, MICHAEL TYNAN, STUART CAMPBELL, ROBERT H ANDERSON

From Guy’s Hospital; King’s College Hospital; and Cardiothoracic Institute, Brompton Hospital, London

Br Heart J 1981

Contemporary Themes

Prenatal screening for congenital heart disease

LINDSEY D ALLAN, DIANE C CRAWFORD, SUNDER K CHITA, MICHAEL J TYNAN

Br Med J 1986
Prenatal Screening in Ontario

- Large geographical area (>1 Mio km²)
- Screening: > 500 clinics and hospitals
Retrospective survey
TOP excluded
97% fetal US scan
5% (N=20) had a fetal CHD diagnosis
Median age: 31wks
2% diagnosed < 24w

Rokoss et al. SickKids 1995
Fetal Cardiac Program Outreach Initiative

Since 1997:

- 1-4 lecture series/year to improve prenatal cardiac screening in Ontario (>3,500 participants)
- Off-site and on-site hands-on training by educator
- Weekly fetal cardiac rounds and multidisciplinary fetal maternal rounds (Teleconference)
- Training of maternal-fetal medicine fellows - 3 months rotations
- Observers and fellows
- Website: www.sickkids.ca/FetalCardiacProgram
Reported Sensitivity of Routine Screening

4-CV

Sensitivity

<40%      > 80%

+ Outflows

+ 3-Vessel View
Earlier Cardiac Evaluation with Improved Imaging

13 wks

week 11

week 40
Referral Criteria for Fetal Echocardiography

- Suspected CHD or unable to visualize heart
- Findings associated with increased risk of CHD:
  - Chromosomal anomalies; CDH; omphalocele; TEF; lung mass; NT>3.5 mm;
  - cystic hygroma; fetal hydrops
- 1st degree relative with CHD
- Fetal arrhythmias: SVT; heart block
- Abnormal cardiac output / vascular resistance:
  - Twin-twin transfusion; A-V malformation; placental failure; masses
- Specific maternal / pregnancy conditions:
  - anti-Ro; poor control of IDDM; phenylketonuria; rubella; parvovirus;
  - certain medication; alcohol; multiple pregnancies; IVF; etc.
Fetal Echoes, Pregnancies Referrals and CHD Diagnosis

median age at CHD diagnosis: 22 weeks (2010)
Evolution in the Prenatal Detection of 9 Common Cardiac Conditions by Fetal Cardiac Program (Tri-Annual Periods)

Cases per 3 years

- VSD
- TGA
- TOF
- Isomerism
- HLHS
- AVSD
- AS/PS
- CoA/IAA
- Arrhythmia

2000-02; N=279
2003-05; N=428
2006-08; N=532
Further improvement in CHD detection rate is possible but may require (the Ministry of Health and Professional Organizations) to set higher standards of practice:

- mandatory training in fetal cardiac imaging
- in U/S equipment and scanning techniques (real time images; addition of 3 vessel views)
Prenatal Referral Rates of HLHS vs. TGA (2009-10)

HLHS: 48/61 (79%)

TGA: 29/63 (44%)

Actively Treated Cases with Fetal vs. Postnatal Diagnosis

HLHS: 22/35 (63%)

TGA: 27/61 (44%)
Prenatal Detection and Live-birth Incidence of HLHS

<table>
<thead>
<tr>
<th></th>
<th>Total Cases</th>
<th>Postnatal</th>
<th>Fetal (live-born)</th>
<th>Fetal Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990-1997</td>
<td>294</td>
<td>187</td>
<td>107 (52)</td>
<td>34%</td>
</tr>
<tr>
<td>1998-2001</td>
<td>122</td>
<td>41</td>
<td>81 (41)</td>
<td>60%</td>
</tr>
<tr>
<td>2009-2010</td>
<td>61</td>
<td>13</td>
<td>48 (22)</td>
<td>79%</td>
</tr>
</tbody>
</table>

- 130,000 births per year in Ontario (1998-2001)
- Live-births with HLHS/year:
  - **Expected** → **Observed**
  - 1990-97: 0.28/1000 → 0.22/1000 LB (n=30/year)
  - 1998-01: 0.23/1000 → 0.16/1000 LB (n=21/year)
  - 2009-10: 0.23/1000 → 0.13/1000 LB (n=17/year)
Actively Managed HLHS with Fetal Diagnosis

Time to surgery (days)       Mid-term survival (years)

$P = 0.005$

$P = 0.9$

$\text{n = 38}$

$\text{n = 14}$
Abnormal Brain Development in Newborns with Congenital Heart Disease

Steven P. Miller, M.D., C.M., Patrick S. McQuillen, M.D., Shannon Hamrick, M.D., Duan Xu, Ph.D., David V. Glidden, Ph.D., Natalie Charlton, B.S., Tom Karl, M.D., Anthony Azakie, M.D., Donna M. Ferriero, M.D., A. James Barkovich, M.D., and Daniel B. Vigneron, Ph.D.

METHODS

We studied 41 term newborns with congenital heart disease — 29 who had transposition of the great arteries and 12 who had single-ventricle physiology — with the use of magnetic resonance imaging (MRI), magnetic resonance spectroscopy (MRS), and diffusion tensor imaging (DTI) before cardiac surgery. We calculated the ratio of N-acetylaspartate to choline (which increases with brain maturation), the ratio of lactate to choline (which decreases with maturation), average diffusivity (which decreases with maturation), and fractional anisotropy of white-matter tracts (which increases with maturation). We compared these findings with those in 16 control newborns of a similar gestational age.
RESULTS
As compared with control newborns, those with congenital heart disease had a decrease of 10% in the ratio of N-acetylaspartate to choline ($P=0.003$), an increase of 28% in the ratio of lactate to choline ($P=0.08$), an increase of 4% in average diffusivity ($P<0.001$), and a decrease of 12% in white-matter fractional anisotropy ($P<0.001$). Preoperative brain injury, as seen on MRI, was not significantly associated with findings on MRS or DTI. White-matter injury was observed in 13 newborns with congenital heart disease (32%) and in no control newborns.

CONCLUSIONS
Term newborns with congenital heart disease have widespread brain abnormalities before they undergo cardiac surgery. The imaging findings in such newborns are similar to those in premature newborns and may reflect abnormal brain development in utero.
Brain Volume and Metabolism in Fetuses With Congenital Heart Disease: Evaluation With Quantitative Magnetic Resonance Imaging and Spectroscopy

_Circulation_ 2010, 121:26-33: originally published online December 21, 2009
Proton MR spectroscopy to measure regional brain biochemistry

↑N-acetyl aspartate and ↓lactate correlate with brain maturation

Fig. 1. A spectrum from a 24 week fetal brain using a PRESS sequence at an echo time of 136 ms. myo-Inositol is seen at 3.5 ppm, choline at 3.2 ppm, creatine at 3.0 ppm, NAA at 2.0 ppm and lactate as inverted bifid peak at 1.3 ppm.

Story L et al. Proton MRS in the fetus Eur J Obs Gyn Reprod Biol 2011;158:3-8
Fetal brain volume = 334 ml

3D Volume MRI to measure brain volume
**Conclusions**—Third-trimester fetuses with some forms of CHD have smaller gestational age– and weight-adjusted total brain volumes than normal fetuses and evidence of impaired neuroaxonal development and metabolism. Hemodynamic factors may play an important role in this abnormal development. (Circulation. 2010;121:26-33.)
Metric Optimized Gating

1. Simulated ECG: R-R_{test}
2. Data: 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 2 2 2 2 3 3 3 3 3 3 3 3 3 ...
3. Image Artifact vs. Heart Rate
4. *metric: “entropy”*
   - Measure of signal scatter in region-of-interest
   - Lower = less scatter, better image

References:
- Atkinson et al. IEEE TMI 1997; 16(6) 903-10
- McGee et al. JMRI 2000; 11(2):174-181
MOG for anatomical cine – Adult volunteers

Conventional ECG gating

Metric optimized gating
Fetal anatomical imaging with MOG
Metric optimized gated phase contrast measurement: main pulmonary artery

Fetal volume: 3326 ml
Fetal weight*: Volume (ml) + 120 x 1.03 = 3549 g

MPA flow= 228 ml/kg/min
Internal validation of fetal flow measurements: MPA + AAO vs DAO + SVC + pulmonary blood flow
### Results of MRI phase contrast with MOG: 12 normal fetuses with Rudolph lamb data for comparison

<table>
<thead>
<tr>
<th>Vessel</th>
<th>MPA</th>
<th>AAO</th>
<th>SVC</th>
<th>DAO</th>
<th>DA</th>
<th>UMBV</th>
<th>PBF</th>
<th>FO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean % &amp; (SD) of CVO by MRI</td>
<td>60 (4)</td>
<td>37 (4)</td>
<td>28 (7)</td>
<td>52 (12)</td>
<td>41 (8)</td>
<td>30 (10)</td>
<td>19* (16)</td>
<td>21* (13)</td>
</tr>
<tr>
<td>% of CVO Rudolph</td>
<td>56</td>
<td>41</td>
<td>31</td>
<td>49</td>
<td>39</td>
<td>39</td>
<td>17</td>
<td>28</td>
</tr>
</tbody>
</table>

*Extrapolated values. DA: Ductus arteriosus, PBF: pulmonary blood flow, FO: foramen ovale
MRI oximetry is possible in the fetus

<table>
<thead>
<tr>
<th></th>
<th>2-D Echo</th>
<th>3D/4D Echo</th>
<th>Fetal MRI</th>
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</thead>
<tbody>
<tr>
<td><strong>Acquisition</strong></td>
<td>Real time</td>
<td>Motion gated volumes (-15s)</td>
<td>Cine imaging: 50s/10 slices</td>
</tr>
<tr>
<td></td>
<td>(Real time)</td>
<td></td>
<td>Phase contrast: 30 s/vessel</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Spectroscopy: 8 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Volumetry: 20 s</td>
</tr>
<tr>
<td><strong>Advantage</strong></td>
<td>Fast</td>
<td>Sharing of examination data</td>
<td>Flow quantification</td>
</tr>
<tr>
<td></td>
<td>Possible &gt; 11 wks</td>
<td>Display of multiple planes</td>
<td>Metabolic information</td>
</tr>
<tr>
<td></td>
<td>Good resolution</td>
<td>Volumetric data</td>
<td>Oximetry ?</td>
</tr>
<tr>
<td></td>
<td>No post processing</td>
<td>Teaching tool</td>
<td>Volumetric data</td>
</tr>
<tr>
<td><strong>Disadvantage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Motion artifacts</td>
<td></td>
<td>Motion artifacts: only &gt;32 w</td>
</tr>
<tr>
<td></td>
<td>Post processing (&lt;1 hr)</td>
<td></td>
<td>Post processing (several hrs)</td>
</tr>
<tr>
<td><strong>Current use</strong></td>
<td>Routine exams</td>
<td></td>
<td>Research</td>
</tr>
</tbody>
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Treatment

Suetonius, 1506
Rationale of Prenatal Treatment

- The rationale for prenatal therapy is to improve survival for conditions in which the fetus is at a high risk for prenatal or neonatal death.

- If death is not imminent but the disease is likely to have major lifelong morbidity, the rationale to treat is that the intervention will modify postnatal outcome sufficiently to justify the potential risks of the procedure.
Pulmonary lymphangiectasia in fetal HLHS/IAS

T2W coronal MRI showing branching fluid filled structures extending out to the lung surface consistent with pulmonary lymphangiectasia

Relation between A-wave Duration and Outcome

Mild: minimal A wave flow reversal

Moderate: A wave 70-90 ms

Severe: A wave >90 ms
Fetal Catheter Intervention for IAS

- **BCH 2/2003:**
  - Figure 1
  - Septum, Narrowed aorta, LA, LV, RA, RV, Balloon catheter

- **BCH 2004:**
  - 6 of 7 HLHS cases (26-34 w) with technically successful BAS resulting in small atrial defects → 1 alive
31 weeks:  
Intact atrial septum  
Obstructive left cardinal vein to CS  
Suspected lymphangangiectasis by fetal MRI
31 weeks:
US-guided fetal catheter intervention at MSH
Mean LA pressure: 15 mmHg
Implantation of a 15 mm coronary stent in IAS
37 weeks: before delivery
<table>
<thead>
<tr>
<th></th>
<th>MRI flow volume (ml/kg/min)</th>
<th>MRI flow volume (ml/kg/min)</th>
<th>Normal flow by CMR (ml/kg/min)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Pre atrial stent 31 weeks</td>
<td>Post atrial stent 35 weeks</td>
<td></td>
</tr>
<tr>
<td>CVO</td>
<td>532</td>
<td>544</td>
<td>548</td>
</tr>
<tr>
<td>SVC</td>
<td>134</td>
<td>122</td>
<td>133</td>
</tr>
<tr>
<td>AAO</td>
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<td></td>
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<tr>
<td>MPA</td>
<td>532</td>
<td>544</td>
<td>337</td>
</tr>
<tr>
<td>PBF</td>
<td>57</td>
<td>87</td>
<td>115</td>
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<tr>
<td>DAO</td>
<td>341</td>
<td>339</td>
<td>259</td>
</tr>
<tr>
<td>PDA</td>
<td>475</td>
<td>457</td>
<td>217</td>
</tr>
<tr>
<td>UMBV</td>
<td>279</td>
<td>198</td>
<td>149</td>
</tr>
</tbody>
</table>

HLHS + IAS
Fetal intervention

Courtesy Mike Seed
Day 3: Stent Removal and Stage 1 Surgery (Norwood)
Outcome of HLHS with Stented IAS

10/2011

Cases (Procedures) N=4 (6)

- Technical Outcome
  - Success N=3 (5)
  - No Success N=1

- Pregnancy Outcome
  - Alive N=3

- Postnatal Outcome
  - Stage 1 N=3
    - N=1: HLHS: died 4 w (PAHT)
    - N=1: HLHS: alive 10 m post Norwood
    - N=1: Cor triatriatum: alive 6 m; hybrid followed by BV repair

Case 1: BAS; RF; Stent
Cases 2-4: Stent

IUD
Conclusion on Prenatal Treatment

- Pharmacological treatment is well established in the management of fetal arrhythmias, with room to further improvement → multicenter trial

- There is much that remains to be learned about the benefits and risks of fetal catheter intervention.