The Fetus as a Cardiac Patient

James C. Huhta, M.D. Perinatal Cardiology

Congenital Heart Institute of Florida Tampa Bay, Florida

Professor, Women’s Health and Perinatology Research Group, Institute of Clinical Medicine, University of Tromso, Tromso, Norway

Professor of Pediatrics, University of Florida, Gainesville, FL

Medical Director, Perinatal Cardiology, All Children’s Hospital
Faculty Disclosure Information

In the past 12 months, I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this CME activity.

I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.
The fetus as a cardiac patient

Data to be Presented:
CHD – in utero transfer
CHF dx and Rx
CHB
Digoxin Treatment
IUGR
Hydrops
SC Teratoma
Perinatal Cardiology
Cardiology for the fetus, child, and mother
Perinatal Cardiology
Cardiology for the fetus, child, and mother
17 week fetus with valve leak
Perinatal Cardiology
Cardiology for the fetus, child, and mother

- Fetal detection of CHD
- CardioAccess allows analysis of the rate of detection of CHD in all patients operated on for CHD.
- At ACH last year detection of CHD prenatally was 35%.
- Goal is improved heart screening education
Fetal detection of CHD
Ductal dependent CHD
- Pulmonary atresia
- TGA
- HLHS
- Critical AS
- Possible coarctation of the aorta
Perinatal Cardiology
Cardiology for the fetus, child, and mother
## CV Profile

### 10-point score

<table>
<thead>
<tr>
<th></th>
<th>NORMAL</th>
<th>-1 POINT</th>
<th>-2 POINTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hydrops</strong></td>
<td>None (2 pts)</td>
<td>Ascites or Pleural effusion or Pericardial effusion</td>
<td>Skin edema</td>
</tr>
<tr>
<td><strong>Venous Doppler</strong> (Umbilical Vein) (Ductus Venosus)</td>
<td>DV (2 pts)</td>
<td>DV</td>
<td>UV pulsations</td>
</tr>
<tr>
<td></td>
<td>UV</td>
<td></td>
<td><a href="#">Graph</a></td>
</tr>
<tr>
<td><strong>Heart Size</strong> (Heart/Chest Area)</td>
<td>≤ 0.35 (2 pts)</td>
<td>0.35 - 0.50</td>
<td>&gt;0.50 or &lt;0.20</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><a href="#">Graph</a></td>
</tr>
<tr>
<td><strong>Cardiac Function</strong></td>
<td>Normal TV &amp; MV RV/LV S.F. &gt; 0.28 Biphasic diastolic filling (2 pts)</td>
<td>Holosystolic TR or RV/LV S.F. &lt; 0.28</td>
<td>Holosystolic MR or TR dP/dt &lt; 400 or Monophasic filling</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><a href="#">Graph</a></td>
</tr>
<tr>
<td><strong>Arterial Doppler</strong> (Umbilical artery)</td>
<td>UA (Normal) (2 pts)</td>
<td>UA (AEDV)</td>
<td>UA (REDV)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><a href="#">Graph</a></td>
</tr>
</tbody>
</table>
Fetal Valve Regurgitation
Tricuspid regurgitation dP/dt

Doppler-Derived Right Ventricular dP/dt

Survivors
Non-Survivors

Ductal Constriction
NIHF
Perinatal Management
Cardiomyopathy

Myocarditis
Genetic syndromes
Inherited defects

Consider transplantation as a neonate
Fetal Congestive Heart Failure

Examples

- CHD with increasing heart size in utero
- Tet absent valve syndrome
- Pulmonary atresia with collaterals
- Ebstein’s malformation
- Critical AS
- L isomerism with CHB
Validation of CVP score—Digoxin Therapy

- Retrospective case series of fetuses with CHF treated with transplacental digoxin, evaluated at baseline (before treatment), weekly during treatment, and prior to death or delivery.
- Mortality of the 28 subjects was 32%.
- First, last, and CVPS after 1 week of treatment predicted survival (odds ratio 2.34, 95% confidence interval 1.10-4.96) with a CVPS of \( \geq 6 \) being the best predictor of survival (sensitivity 0.83, specificity 0.75).
- All fetuses that died had notching of the umbilical venous flow.
- The overall CVPS increased from baseline during treatment \( (p = 0.003) \) in all subjects.
- The CVPS score is useful in assessing therapeutic effects of digoxin in the fetus with multiple etiologies for CHF.

Digoxin Therapy for the fetus in CHF

Structural cardiac defects (n= 21) or noncardiac anomalies (n=7)

Length of treatment (5.0 ± 3.2 weeks)

<table>
<thead>
<tr>
<th>Non-cardiac Defect</th>
<th>Cardiac Defect</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Cystic hygroma, XO</td>
<td>*Ebstein’s malformation (3)</td>
</tr>
<tr>
<td>*Sacroccocygeal tumor</td>
<td>*TOF, absent pulmonary valve (5)</td>
</tr>
<tr>
<td>Recipient TTS (5)</td>
<td>*Critical AS and AVVR (6)</td>
</tr>
<tr>
<td>Cerebral AVM</td>
<td>*Cardiomyopathy</td>
</tr>
<tr>
<td></td>
<td>Subaortic Rhabdomyoma</td>
</tr>
<tr>
<td></td>
<td>*Critical PS, TVD</td>
</tr>
<tr>
<td></td>
<td>TA, TGV severe PI</td>
</tr>
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<td></td>
<td>* PA, IVS</td>
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<td></td>
<td>*HLHS, EFE</td>
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</tbody>
</table>

* Hydrops

**Patient Population Treated with Digoxin**

* = hydrops
Mean Composite CVPS as Predictor of Prenatal Survival

- Baseline: 4.3, Non-survivor: 7.3, Perinatal Survivor: 4.3
- After Digoxin: 7, Non-survivor: 7, Perinatal Survivor: 3.7
- Pre delivery or demise: Non-survivor: 7, Perinatal Survivor: 7

- Graph shows mean composite CVPS values with error bars for non-survivors and perinatal survivors at different stages: baseline, after Digoxin, and pre delivery or demise.
Results

- Mortality was 32%, and limited to those with moderate (3/13) and severe (6/9) CHF.
- A CVPS of $\geq 6$ was the best predictor of survival (sensitivity 0.83, specificity 0.75).
- All fetuses that died in utero had notching of the umbilical venous flow.
- The first, last and CVPS after 1 week of treatment predicted survival (Odds ratio 2.34, 95% CI 1.10-4.96).
Results

• The overall CVPS increased from baseline during treatment ($p = 0.003$) in all subjects.
• The CVPS score is useful in assessing therapeutic effects of digoxin in the fetus with multiple etiologies for CHF
Fetal CHD

- CHD prognosis is linked to maturity
- Premature delivery is the highest risk factor for the newborn with CHD
Fetal CVP Score - 146 fetuses

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
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<tbody>
<tr>
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<tr>
<td><strong>For Mortality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.25</td>
<td>0.98</td>
<td>0.88</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>For 5 minute Apgar score &lt;=6</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.22</td>
<td>0.98</td>
<td>0.75</td>
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</table>
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Validation of CVP score

Disease-specific applications of CVP score in fetal right heart disease

- Ebstein Malformation
- Pulmonary atresia – IS
- Tricuspid valve dysplasia
- Critical pulmonary stenosis
Cardiovascular profile score in fetal right heart defects Ana L. Neves et al.

- Fetal echocardiogram exams (143) from 28 patients were analyzed, ranging from 1 to 13 echocardiogram (median of 4).
- The mean ± SD gestational age at the delivery was 37 weeks ± 2, the mean ± SD birth weight was 2705 g ± 677, and the median Apgar scores at 1 and 5 min ranged between 1-9 (8) and 5-9 (8), respectively.
- Twenty-five of the 28 fetuses were born alive. The total perinatal mortality was 14/28 (50%).
Perinatal Cardiology
Fetal R heart CHD

Cardiothoracic ratio

CVP score

Non-survivors  Survivors

Non-survivors  Survivors
• The observed Odds Ratio of 0.9252, (95%CI: 0.866, 0.988) indicates that a higher CVP score is a protective factor for risk of death. The CVP score is an indicator of risk of death, meaning that for each 1-point score reduction of the CVP, there is an additional 8% risk of death.

• The strongest observed association was between the cardiothoracic ratio and risk of death. The observed OR of 2.7933 (95%CI: 1.237 to 6.309) indicates for each unit of increase in the CTR ratio results in nearly a 3-fold increased risk of death in fetuses examined for this investigation.

100 hydropic fetuses
CVP score range-last exam  3-10
6 died-Average CVP score 6 versus 7
Validation of CVP score-Hydrops

21 pregnancies were terminated (21%).

54 of the remaining 81 fetuses survived (67%) and perinatal death occurred in 27 fetuses (33%).

CVP score 6 (IQR 5-6) in cases with perinatal mortality and 7 (IQR 4-8) p<0.035
The best predictor for an adverse outcome was the venous Doppler sonography of UV and DV, in particular umbilical venous pulsations.
Validation of CVP score-Hydrops

The longitudinal study showed a survival rate of 49/72 (68%) and a PNM of 23/72 (32%) after exclusion of 6 terminated pregnancies.

CVPS decreased a median of 1.5 points in those who died (IQR 0.25-2.75) p<0.001

CVPS increased a median of 1.0 points in those who lived (IQR 0-2) p<0.001
Validation of CVP score- Sacrococcygeal Teratoma

To determine the value of CVP Score for the prognosis of the fetus with SCT

26 fetuses with SCT;

CVP score of survivors was 9 (range 8-10)

CVP in nonsurvivors was 7 (range 4-9) p<0.004

Respondek et al. ISUOG Abstract Sept. 2005
Validation of CVP score-IUGR

- Neonates with 5-minute Apgar scores ≤ 7 had lower CVP scores than with scores > 7 (6 (2-10) vs. 9 (5-10), p<0.001)

- Umbilical artery NT-proANP levels of newborns with CVP score ≤ 6 were greater (5208 (2850-16030) pmol/L) than the levels of neonates with CVP exceeding 6 (1626 (402- 9574) pmol/L), p=0.0001).

- All NT-proANP values of newborns with CVP score ≤6 were above the 95th percentile NT-proANP value in normal pregnancies, while 42 out of 67 (63%) fetuses with CVP > 6 showed NT-proANP concentrations exceeding the 95th percentile value in normal pregnancies.

- Umbilical artery NT-proANP values correlated inversely and significantly with CVP score values.
### Summary: CVPS Associated with Mortality

<table>
<thead>
<tr>
<th>Group</th>
<th>Perinatal Mortality</th>
<th>CVP score</th>
<th>Mortality* or Early Delivery**</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (CHD)</td>
<td>20%</td>
<td>&lt;7</td>
<td>*87.5% vs. 15.2%</td>
</tr>
<tr>
<td>2 (Hydrops)</td>
<td>60%</td>
<td>&lt;7</td>
<td>*73.5% vs. 26.5%</td>
</tr>
<tr>
<td>3 (IUGR)</td>
<td>11%</td>
<td>&lt;6</td>
<td>100%</td>
</tr>
<tr>
<td>4 (AVB)</td>
<td>*82%, **26%</td>
<td>&lt;7</td>
<td>*100%, **100%</td>
</tr>
<tr>
<td>5 (Digoxin)</td>
<td>32%</td>
<td>&lt;5</td>
<td>100%</td>
</tr>
</tbody>
</table>
## Component Markers Associated with Mortality

<table>
<thead>
<tr>
<th>Group</th>
<th>Component Markers</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (CHD)</td>
<td>Hydrops, Cardiomegaly</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>2 (Hydrops)</td>
<td>Abn venous D</td>
<td></td>
</tr>
<tr>
<td>3 (IUGR)</td>
<td>Abn venous D Abn function</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Cardiomegaly</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.008</td>
</tr>
<tr>
<td>4 (LAI-AVB)</td>
<td>Hydrops Cardiomegaly</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.003</td>
</tr>
<tr>
<td>5 (Digoxin)</td>
<td>Abn DV D Hydrops</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.01</td>
</tr>
</tbody>
</table>
The perinatal outcome of fetal congenital heart defects is worse than that observed for postnatally identified infants. A possible explanation is the relatively high incidence of aneuploidy and extracardiac anomalies in fetal cases.
The fetus as a cardiac patient

Data to be Presented:
- CHD
- CHF dx and Rx
- CHB
- Digoxin Treated
- IUGR
- Hydrops
- SC Teratoma
Ductus venosus agenesis

Digoxin treatment

CVP score from 7 to 9/10
Fetal therapy has the potential for 200% mortality.

Early intervention could change the natural history of disease.

Mother must be a willing participant.
Technique – Fetal Aortic Valvuloplasty

- 5 dimensional procedure
- 3 spatial dimensions
- Beating heart
- Moving fetus

- 2D ultrasound
- Dilated LV, ↓ function
- Fetus paralyzed and held in position
Fetal Aortic Valvuloplasty for AS with Evolving HLHS

- Procedures Attempted: N=65
  - Success: N=50
    - Not Live Birth: 5
      - HLHS*: N=27
    - Viable Live Birth: N=43
      - Biventricular Circulation: N=15
  - Failure: N=15
    - Not Live Birth: N=3
    - Viable Live Birth: N=12
      - HLHS: N=11
        - *2V
          - N=1
        - Born 35w

- In Utero: N=2
- Pregnancy Outcome
- Postnatal Outcome

Update May, 2008
Postnatal LV growth
s/p fetal intervention at 22w

Birth 22mo  s/p 2V repair
Perinatal program future research and development

- 3-D imaging
- First Trimester diagnosis and counseling
- Fetal ECG and Holter monitoring
- Fetal MRI
- Fetal intervention to prevent preterm labor
Florida... The Plywood State
Advances in Perinatal Cardiology
9th Annual Fun in the Sun Course

Oct. 4-7, 2012
St. Petersburg, FL

Focus: Form and function in Perinatal Cardiology

See www.allkids.org

“Conferences”
Perinatal Cardiology

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Professor of Pediatrics, University of Florida
Tampa Bay, Florida