LVOTO Data Collection: Lessons Learned from 1st CHSS Study with Remote Data Collection*

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Study Proposal: Impact of Aortic Arch Obstruction and Intervention for Aortic Arch Obstruction on Clinical Outcomes and Echocardiographic Parameters, Including Systemic Ventricular Function and Atrioventricular Valve Regurgitation in Neonates with Critical LVOTO Undergoing the Norwood Operation

Pirooz Eghtesady and Tara Karamlou
Feasibility of Existing Serial Echo and Cath Data to Predict a Decision for Aortic Arch Intervention in Neonates with Critical LVOTO Following the Norwood Operation

Pirooz Eghtesady and Tara Karamlou, and Members of the Working Group

CHSS Spring Work Weekend April 2017
Analysis Plan

1) Construct a flow-chart of arch events;

2) Ascertain the completeness of echo and cath data regarding arch information needed to define intervention

3) Initial biopsy to define concordance of echo parameters with subsequent surgical or cath intervention for arch obstruction
Dataset

Critical LVOTO – Norwood reconstruction only
exclude hybrid patients;
biventricular or transplant censored at time of conversion;

Time-frame biopsied was between Norwood reconstruction and up to Stage 2

Serial echo and cath data on all patients undergoing intervention were entered over past 6 months

Clinic data was also recorded serially
128 arch procedures among 99 patients up to BDG
# Preliminary Data

<table>
<thead>
<tr>
<th></th>
<th>Initial Procedure is Norwood (N=579)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-intervention rate (in patients with a Norwood as their 1\textsuperscript{st} procedure)</td>
<td>17% (99/579)</td>
</tr>
<tr>
<td>Overall survival in those with an arch re-intervention</td>
<td>86% (85/99)</td>
</tr>
<tr>
<td>Total Number of arch re-interventions after Norwood</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>76% (75/99)</td>
</tr>
<tr>
<td>2</td>
<td>24% (24/99)</td>
</tr>
<tr>
<td>3</td>
<td>4% (4/99)</td>
</tr>
<tr>
<td>4</td>
<td>1% (1/99)</td>
</tr>
<tr>
<td>Types of procedures</td>
<td></td>
</tr>
<tr>
<td>Catheter (balloon dilatation or stenting)</td>
<td>81% (104/128)</td>
</tr>
<tr>
<td>Operative (Stage 2 or interval)</td>
<td>19% (24/128)</td>
</tr>
</tbody>
</table>
## Baseline Comparisons

<table>
<thead>
<tr>
<th>Variable</th>
<th>Arch intervention</th>
<th>No arch intervention</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight</td>
<td>3.2 +/- 0.4</td>
<td>3.1 +/- 0.6</td>
<td>0.2</td>
</tr>
<tr>
<td>Prenatal diagnosis</td>
<td>35%</td>
<td>33%</td>
<td>0.4</td>
</tr>
<tr>
<td>Female</td>
<td>37%</td>
<td>32%</td>
<td></td>
</tr>
</tbody>
</table>

Needed data to incorporate for next steps:
1) anatomic factors (initial arch sizes measurements),
2) surgical factors
3) others (noncardiac anomalies, genetics?)
Variables of Interest

• Echo:
  – Mean gradient
  – Mean velocity
  – Peak gradient
  – Peak velocity (converted to pressure with Bernoulli eq)

• Cath data:
  – Peak-to-peak gradient
  – Degree of obstruction relief

• Clinic data
  – Non-invasive four extremity BP measurements
Background

Last Fall work weekend, we presented an initial feasibility study relating serial echo and cath data obtained from submitted reports with the clinical outcome of re-intervention for neo-aortic obstruction following the Norwood operation.

A biopsy of patients were chosen who had arch re-intervention.

We determined the prevalence of re-intervention was also thought to be important, as well as the ‘timing’ relative to staged palliation.
Feasibility Aims

1) Describe the prevalence of arch intervention between Norwood operation and bidirectional Glenn

2) Describe the timing of arch intervention following Norwood operation

3) Determine the quality and quantity of serial echo and cath data among patients undergoing arch intervention
Feasibility Aims

4) Determine whether serial echo and cath data from submitted reports accurately predict a decision for arch intervention between Norwood and Stage 2?

5) Based on discussion last work weekend, it was felt that we ought to focus solely on a hard endpoint of re-intervention.

6) Needed to assess the entire cohort rather than subset that had re-intervention: need to complete data collection.
Possible Metrics

Possible echocardiographic metrics:
- Peak and/or mean gradients
- Coarctation index
- Subjective report of ‘obstruction, stenosis, or flow acceleration across reconstructed arch

Possible clinical metrics:
- Non-invasive BP gradients from clinic or hospital notes

Possible cath-based metrics:
- Cath gradient (peak); Angiographic narrowing

Composite Metric: BP gradients $\geq -20$ mmHg
- Peak arch velocity $\geq 3.5$ m/s echo
- Cath peak-to-peak $\geq 20$ mmHg
Quality/Quantity of Echo Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Mean +/- SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak velocity (m/s)</td>
<td>358</td>
<td>24 +/- 14</td>
</tr>
<tr>
<td>Peak gradient (mmHg)</td>
<td>471</td>
<td>32 +/- 15</td>
</tr>
<tr>
<td>Mean gradient (mmHg)</td>
<td>460</td>
<td>19 +/- 8</td>
</tr>
</tbody>
</table>

Among 99 patients with arch obstruction, N= 15 had no echo measurements
Median number of echo measures = 2 per patient
Maximum number of echoes per patient = 13
Quality/Quantity of Cath Data

• Peak-to peak gradient: N=337

• Mean 21 +/- 16 (0 - 70 mmHg)

• Median number of cath measures per patient was 1, with a maximum of 4.
Next Steps

• Complete data collection and entry for entire cohort
• Multivariable analysis to identify other factors associated with arch re-intervention
• Identify trends in arch gradients over time and whether these time-trends are associated with intervention
• Integration of serial arch data into existing longitudinal models of ventricular function and tricuspid valve function
So... We Needed to Complete Data Collection

• Tremendous amount of data
• Difficult to settle on definitions and variables of interest (i.e. how can we limit the volume of data collection?)
• Idea of remote data collection was mentioned

• But – there were difficulties with this approach (data integrity, validity, security with transfer, lessons from PC study**)
Issues with Remote Data Collection

- Bring the coordinators on board with the development of the variables to be collected (what may be easy for us to understand, such as the peak to peak, may not be for them as they have varying backgrounds)

- Are we only including coordinators whose surgeons are members of the working group

- Surgeons must be aware of the time consumption of data abstraction and the impact it will have on their other work
Issues with Remote Data Collection

- Once variables have been decided on, collect data for one-two weeks then regroup with coordinators to discuss any potential issues, continue to have routine meetings until completion of data abstraction.

- Put a process in place to verify that the data they are abstracting from is the same that they have sent to the data center in case there is a need to revisit it in the future.
Issues with Remote Data Collection

- Be clear about deadlines and the reason for them, it would be very difficult for the data center to abstract a great deal of information from a site last minute if that site /coordinator cannot complete their abstraction.

- Determine a way to acknowledge the work coordinators have contributed to the project.

- The coordinators must assign their subjects enrolled in the study their screening numbers as in the future we will not be able to put the subjects name/birthdate on spreadsheets to collect data and if we move to REDcap data collection for them we cannot use that PHI.
Where Are We Now?

- Past August, we finalized data collection plan
- Teleconference with the remote data coordinators... (suboptimal timing)
- Over course of several phone conferences with working group members, finalized abstract
- Abstract submitted to AATS (Paul presenting data tomorrow)
Arch Interventions After Norwood and Before or during Stage II Procedure

Arch interventions
N=151

119 patients

Catheter*
N=115
(21 at pre-stage II cath)

100 patients

Surgical*
N=36

33 patients

Balloon Dilation
N=112

Stenting of Coarctation
N=4

Isolated Arch Repair
N=14

Concurrent with SVCPA
N=17

Concurrent with HTX
N=3

Concurrent with Yasui
N=2
Questions/Discussion
## Associations Between Variables and Intervention

<table>
<thead>
<tr>
<th>Variable</th>
<th>Beta</th>
<th>SE</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak velocity M/s</td>
<td>0.04</td>
<td>0.02</td>
<td>0.005</td>
</tr>
<tr>
<td>Peak arch gradient (m/s)</td>
<td>0.03</td>
<td>0.02</td>
<td>0.14</td>
</tr>
</tbody>
</table>
Critical LVOTO
Overall Cohort
N=924

Eligible
N= 852

Excluded
N= 72

Definitive First
procedure
N=785

Death before
“definitive”
procedure
N=13

Alive and enrolled
without surgical
data entered
N=54

Norwood
N=534

Norwoods who
Underwent an Arch
procedure
N=115

Arch procedure
after Norwood &
before Stage 2
N=89

Stage 2
N=100

Arch procedure at
Stage 2
N=8

Dead
N=5

Fontan
N=69

Dead
N=11

Arch procedure
after Fontan
N=1

Dead
N=4

Updated March 9, 2016
Arch Re-obstruction cohort
and procedure sequence