Caring for Adults with Congenital Heart Disease
Where Are We Going?

Michael Landzberg, MD
Boston Adult Congenital Heart (BACH) Group

25th “Advances in Heart Disease” – San Francisco
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Disclaimers: Michael J. Landzberg, MD

• Research/Grants: Actelion, Gilead, NMT
• Consultant: Actelion, NMT
Liberty Leading the People

François Delacroix
Alfred Blalock, Helen Taussig, and Vivien Thomas
# Caring for Adults With Congenital Heart Disease

- Where have we been
  - epidemiology
  - resource utilization
  - loss to care
  - training

- The RV

- Heart failure and arrhythmia

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetralogy of Fallot</td>
<td>valves</td>
</tr>
<tr>
<td>Aortic coarctation</td>
<td>stents</td>
</tr>
<tr>
<td>Atrial septal defects</td>
<td>devices</td>
</tr>
</tbody>
</table>

1) Care Guidelines  2) Accreditation
Hannah:
• 34 yo I-Banker, NYC ↔ SF
• **TOF**, complete repair age 4 mo, periodic follow til age 14 → “success”
• Syncope (facial lac) unpacking home→ ER: “vasomotor”. “WHO FC I” (II) New PCP sends to you
• BMI 30, 150/90 70 JVP > 12 (“v”) sat 98% scoliotic clear lungs prom RV, S3, PR and TR, liver edge, ascites, edema
• SR, QRS 180 ms CRBB
Tetralogy of Fallot ("monology"):

- Ventricular septal defect
- Pulmonary stenosis
- Right ventricular hypertrophy
- Overriding aorta
Tetralogy of Fallot (repaired):

- VSD closure
- Relief of RVOTO:
  - Infundibular muscle resection
  - Transannular RVOT patch
  - RV to PA conduit
Tetralogy of Fallot

• Most common form of cyanotic CHD (5-6%)
• Excellent survival after repair
  < 2% early mortality
  20 year survival approaches 90%, then
• Late morbidity and mortality
  Risk of death triples in the 3rd post op decade
  Right heart failure
  Atrial and ventricular arrhythmias
  Sudden death: QRS duration
Tetralogy of Fallot

Hannah: “Do Outcomes Vary with Gender?”

↑pulmonary regurgitation

- Regurgitant orifice
- RV dilation
- Diastolic $\Delta$ (PA-RV)
- PA-RV “coupling”
- Duration of Diastole
- Neurohormonal activation
- Sympathetic activation

- Compliance of PA’s
- Capacitance of PA’s
- PA dilation/aneurysm
- LV function
- Compliance of RV
- Capacitance of RV
- RV dilation/aneurysm
- RV contractility

LV function
PR timeline

compensation failure dilation irreversible injury

 ↑ PR

↑ RV loading

eRV hypertrophy

RV dilation

RV ischemia

RV failure and ↓ Systemic perfusion

Ectopy

Neurohormonal, Cytokine, Mechanical Stretch Signalling

Toxicity, ischemia or energy depletion

Altered Gene Expression

Growth and remodelling

Apoptosis

Necrosis

Cell and Organ Death

15-35 yrs
Phases of RV Dysfunction (cMRI)

\[ \text{RV EF} = 2.26 + 0.76 \times \text{LVEF} \]

\[ r = 0.58 \]

\[ p < 0.001 \]
Survival After PVR

- Dharigés B et al. JThorac Cardiovasc Surg 2001

Diagram: Survival analysis with time in years and freedom from death percentage.
Valve Failure After PVR

Is There a “Point of No-Return”?  

RV function: Early vs Late Repair of ASD

Celik S et al. Jpn Heart J 2004
Is There a “Point of No-Return”? 

RVEDV (cMRI): PVR in TOF

Therrien J et al. Am J Cardiol 2005
Is There a “Point of No-Return”?  

RVEDV (cMRI): PVR + RV reduction in TOF  

Oosterhof et al. Circulation 2007
Is There a “Point of No-Return”?

Waiting for Symptoms: “Success” of PVR in TOF

Timing for PVR: 2008

- Moderate-severe PR ≥ 25%
- ≥2 of the below
  - RVEDV ≥ 160 (150) ml/m² (Z ≥ 5)
  - RVESV ≥ 70 ml/m²
  - RVEF ≤ 45%
  - LVESV ≤ 65 ml/m²
  - Sxs (WHO FC, NHA, meds, VT)
  - RVOT aneurysm
- Other hemodynamic issues
- Late (≥ age 3 yrs) repair

Knauth AL et al. Heart 2008
Ohuchi H et al. Circulation 2000
Cardiac autonomic nervous activity after RVOT reconstruction
Fredriksen PM et al. Am J Cardiol 2001

Correlation of heart rate (neurohormal activation) and $MVO_2$
CHD as the prototype of heart failure syndrome
Prognostic value of GFR in all ACHD
Prognostic value of anemia in all ACHD
MVO2 \propto CO \times C (a-v)O_2
Fontan: Functional Status (MVO$_2$)

Mean ± SD
- Aortic coarction: 28.7 ± 10.4
- Tetralogy of Fallot: 25.5 ± 9.1
- VSD: 23.4 ± 8.9
- Mustard-operation: 23.3 ± 7.4
- Valvular disease: 22.7 ± 7.6
- Ebsteins anomaly: 20.8 ± 4.2
- Pulmonary atresia: 20.1 ± 6.5
- Fontan-operation: 19.8 ± 5.8
- ASD (late closure): 19.2 ± 6.2
- ccTGA: 18.6 ± 6.9
- Complex anatomy: 14.6 ± 4.7
- Eisenmenger: 11.5 ± 3.6

ANOVA p<0.0001

Giardini A et al. Am Heart J 2007
CircP (MVO2 x Peak HR): ACHD
ACHD Survival
Effect of $V_E/V_{CO2}$ slope

MDE in repaired TOF

- 92 patients s/p TOF repair
- RV MDE in all patients
- LV MDE in 53%

MDE related to:
- Ventricular dysfunction
- Exercise intolerance
- Neurohormonal activation

Babu-Narayan S. Circ 2006; 113: 405
RV Regional Wall Motion 3D Model

Wald R. Work in review

- Regional wall motion abnormalities correlated with MDE (P=0.002) and were primarily in the RVOT
- Segmental dysfunction and MDE in the RVOT were associated with symptoms (p = 0.018)
Observe / Examine
(ACHD: “master clinicians”)
- Arterial waveform: PP
- BMI
- LEAP (systemic veins) + JV W’s
- Chest movement
- Palpation
- Presence of shunt flow
- Thyroid

Serologies
- Creatinine
- Uric Acid
- BNP
- Hct / Hgb
- BS / chol

Exercise
- EKG: CPET
- MVO2
- VE/VCO2
- O2 pulse
- HRR
- Rhythm

Volumes (Imaging)
- CXR
- TTE/TEE
- Integrative (flow v scar)
- ? diastology
- ? twists

Invade
- Measure all
- Pericardium
- ? Load
- ? PV loops
- ? PWA
- ? Intervention
Tetralogy of Fallot (repaired):

- VSD closure
- Relief of RVOTO:
  - Infundibular muscle resection
  - Transannular RVOT patch
  - RV to PA conduit
Melody™

- Bovine Jugular Venous Valve Segment
- Platinum-Iridium Stent
Acute Effects on Ventricular Size / Function

<table>
<thead>
<tr>
<th>RV Measures ↓</th>
<th>Pre</th>
<th>Post</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDV ml/m²</td>
<td>117 ± 30</td>
<td>94 ± 29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESV ml/m²</td>
<td>56 ± 25</td>
<td>53 ± 27</td>
<td>n.s.</td>
</tr>
<tr>
<td>Eff SV ml/m²</td>
<td>36 ± 9</td>
<td>45 ± 9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EF %</td>
<td>54 ± 12</td>
<td>53 ± 11</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LV Measures ↑</th>
<th>Pre</th>
<th>Post</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDV ml/m²</td>
<td>67 ± 16</td>
<td>72 ± 14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESV ml/m²</td>
<td>28 ± 9</td>
<td>29 ± 9</td>
<td>n.s.</td>
</tr>
<tr>
<td>Eff SV ml/m²</td>
<td>37 ± 8</td>
<td>44 ± 7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EF %</td>
<td>59 ± 7</td>
<td>63 ± 6</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Frigola et al, Circulation 2008
Short-term Effect on Cardiopulmonary Function

Peak VO₂

Bonhoeffer, London/Paris

p<0.001

n=99
1-Year Effect on Cardiopulmonary Function

Frigola et al, Circulation 2008

VE/VCO2 36 → 34
Ventricular shape: function arterial coupling
The Tip of the Iceberg
Hannah:

• 34 yo I-Banker, NYC ↔ SF
• TOF, PR, syncope: Vstim (+) + QRS → ICD and percutaneous PVR
• Weight loss, exercise, improved BP and BS control
• Return to coordinated continuous long-term care, leads national advocacy group
ACHD: Multiple Layers of Extracardiac Interaction

- Peripheral vessels
- Lung parenchyma
- Kidneys
- Liver
- Intestines
- Musculoskeleton
- Neuro-hormonal Δ’s
- Endocrinologic Δ’s
- etc…………
**ACHD Survivors: Multisystem Comorbidities**

**Incidence of Obesity**

*(n=54%)*

BACH “Main”

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>14 months</th>
<th>n = 684</th>
<th>mean age 36.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke and transient ischaemic attack</td>
<td>34%</td>
<td>7.6</td>
<td>6.1 to 9.3</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>20%</td>
<td>3.4</td>
<td>2.3 to 5.1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.3</td>
<td>1.1 to 1.5</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>46%</td>
<td>1.1</td>
<td>0.9 to 1.2</td>
</tr>
<tr>
<td>1.9</td>
<td>1.1 to 1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.1</td>
<td>7.1 to 7.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.7</td>
<td>5.2 to 8.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.4</td>
<td>1.3 to 1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.6</td>
<td>2.2 to 3.2</td>
<td></td>
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2-3x ↑ hospitalizations ↑ in all hospital resources
(use is related to cardiovascular pathology as well as age)

↓ total elective admissions with ↑ age

↑ ER / total admissions with ↑ age

In the “Natural History Study”, 40% of patients with AS/PS/VSD had not had a cardiac examination in over 10 years.

Second Natural History Study
Of ACHD’ers transitioning to level 3 care, more than 25% had not had a single evaluation after their 18th birthday.

• > 1/3 cardiology fellowships offer < 3 lectures in ACHD
• 11 programs (9 adult, 2 pediatric) offer specific ACHD training
• 42 (31 adult, 11 pediatric) fellows (0.5/100) in the past 10 yrs have “full” ACHD training (estimated 250 specialists x 1000 patients each required)

ACHD Care: A failure of success?
Jackie Sue:

• 32 yo f marathoner, newly recognized systemic HTN: BB

• 140/90 (upper) 110/80 (lower), minimal (+) rad-fem pulse delay, posterior m, ao click, no S4

• MRI: min LVH, nl LV fn, mildly narrow AoDt post isthmus: referred for dilation / stent

• Cath: PCW: 12, LV 115/12: AoAs 140/80: AoDT 100/80 CI 3.2 l/min/m-2
Jackie Sue:

- 32 yo f marathoner, newly recognized systemic HTN: BB
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- Cath: PCW: 12, LV 115/12: AoAs 140/80: AoDT 100/80 CI 3.2 l/min/m-2

What do we do?
• 5% congenital cardiac lesions (0.2/1000 live births)
• 1.3-2: 1 male / female
• Associations: BAV, HLHS, VSD, ICA, Turner’s
• 5% congenital cardiac lesions (0.2/1000 live births)

• 1.3-2: 1 male / female

• Associations: BAV, HLHS, VSD, ICA, Turner’s

• Normal growth / development, weak, delayed pulses, sHTN (± exercise), HA, claudication, late-systolic loading/ventriculo-arterial coupling abnormalities and their sequelae
Etruscan remains: Aortic coarctation and rib notching in mid 40’s yo (5th-6th century BCE)
Campbell M. Br Heart J 1970.

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**Untreated Natural Survival: AoCo**

- Paris 1791
- Abbott 1928
  - n = 200, ↓ 42 yrs, rupture, SBE, CNS hemorrhage
- Reifenstein 1947
  - n=104, ↓ 35 yrs, rupture, SBE, CHF, CNS hemorrhage

<table>
<thead>
<tr>
<th>Years of Age</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>75%</td>
</tr>
<tr>
<td>32</td>
<td>45%</td>
</tr>
<tr>
<td>46</td>
<td>20%</td>
</tr>
<tr>
<td>58</td>
<td>10%</td>
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</tbody>
</table>
CAN I?
CAN I?  SHOULD I?
AoCo: Late Outcomes

- Death
- Functional Incapacity
- “CHF” (contractility, ↑ EDp)
- HTN (rest, exercise)

- Atherosclerosis / vascular fn
- Vascular site integrity
AoCo: Late Outcomes

- Death
- Functional Incapacity
- “CHF” (contractility, ↑ EDP)
- HTN (rest, exercise)

- Atherosclerosis / vascular fn
- Vascular site integrity
“Post-repair”: Vascular function

Xu J et al. Am Heart J 1997 (IVUS)
“Post-repair”: FMD and GTN-D

“Post-repair”: FMD and GTN-D

Post-repair: LSL, V-A Coupling

“Post-repair”: ↑ LV Mass

“Post-repair”: Aortic Pathology

Ao pathology in 60 / 124 survivors (35 ≥ 40 mm)

Appeared independent of HTN, residual AoCo
<table>
<thead>
<tr>
<th>What We Should Not Do</th>
<th>What We Should (Must) Do</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Registry: IMPACT</td>
</tr>
<tr>
<td>Standardize</td>
<td></td>
</tr>
<tr>
<td>Understand complications</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Randomized Study: Multi-center</td>
</tr>
<tr>
<td>BA / stent v surgery v med Rx + exercise</td>
<td></td>
</tr>
<tr>
<td>Standardized Rx, X-over, follow Outcomes</td>
<td></td>
</tr>
<tr>
<td>Technical: acute / reop</td>
<td></td>
</tr>
<tr>
<td>EC / vasc anatomy + function</td>
<td></td>
</tr>
<tr>
<td>HTN control (rest, exert)</td>
<td></td>
</tr>
<tr>
<td>LV mass, CHF, sleep</td>
<td></td>
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<tr>
<td>Electro-mechanical</td>
<td></td>
</tr>
<tr>
<td>Sxs, functional capacity</td>
<td></td>
</tr>
<tr>
<td>Atherosclerosis / death</td>
<td></td>
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</table>
Referral:

• 81 years old: short of breath

• Hypertension, now WHO III (moderate symptoms at low activity)

• as child: “hole in the heart: no need to fix or follow” → lived “a good and meaningful life, with more yet to do”

• Echo: enlarged RV, hypokinetic, RVVO 22 mm ASD-2, left to right flow

10% of all (20 – 40% in adults) CHD
RV Volume Overload

\frac{Q_p}{Q_s} \geq 1.5

10% of all (20 – 40% in adults) CHD
Secundum ASD: Untreated

- ↑ risk PHT
- ↑ risk A Fib

ASD-2: Catheter Closure

Improved R ⇔ L heart
↓ R-heart size  ↑ LVEF

Eccentricity 2004
Diastolic Function 2004
Myocardial Performance Index 2005

2-ASD Closure: ↓ AF

Preprocedural AT  
Age > 55 years

ASD-2 Closure: $\uparrow$ MvO2

Brochu. Circulation 2002

Giardini. J Am Coll Cardiol 2004

Correlates with LVEF

Correlates with Qp/Qs
Closure Benefit: CE (RCT)

Device Evolution
> 95% of all secundum ASD can be closed via catheterization.

Referral:

• Diuresis
• Improved shortness of breath
• She now does all she wants to do
• She still has atrial fibrillation
• Do you still close her ASD? →
The decision is complex
ASD-2: Points

1. AHA guidelines: I B
   Indication: RVVO

2. Despite attempts at data collection, we still live in a world of BIAS

3. Surgery: AFib / TR / CAD
Caring for Adults With Congenital Heart Disease

Tetralogy of Fallot
Aortic coarctation
Atrial septal defect

Failure of Success
Heart failure “model”
Coordinated follow
RV as a determinant
PR $\propto$ volumes + sxs
HTN: rad-fem delay
ASD’s: RVVO (1b)

Care Guidelines
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