UNIQUE ASPECTS OF HEART FAILURE IN ADULTS WITH CONGENITAL HEART DISEASE

CONNECTICUT ADULT CONGENITAL HEART SERVICE, CONNECTICUT CHILDREN'S MEDICAL CENTER & HARTFORD HOSPITAL

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DISCLOSURES: NONE
CONGESTIVE HEART FAILURE IN ADULT CONGENITAL HEART DISEASE

1. Scope of the problem
2. Case
3. Causes of Heart Failure in Congenital Heart Disease
4. Ventricles in Congenital Heart Disease
   - Systemic ventricular dysfunction (LV or RV morphology)
   - Sub-pulmonary ventricular dysfunction
   - Single ventricular dysfunction
5. Neurohormonal aspects and Biomarkers
6. Management approach
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5. **Neurohormonal aspects and Biomarkers**
6. **Management approach**
Survival to 18 yrs of Age with *Complex* CHD

- 1980: 80%
- 1970: 50%
- 1960: 15%
- 1940: 5%

1% d-TGA and 10% of TOF to adulthood

Warnes C. J Am Coll Cardiol 2001
Ven der Velde ET Eu J Epidem 2005
CHD PATIENTS REACHING ADULTHOOD

Adult CHD Patients


Hoffman 1978 Kaiser
Fyler 1980 New England
Ferencz 1985 Baltimore-DC

20,000-40,000 new patients/yr
5-10% increase/yr

325,000
500,000
750,000
1,000,000
1,500,000
ACHD CLASSIFICATION

• Mitral Atresia
• d-TGA
• CCTGA
• DORV
• Heterotaxy
• Single V
• Conduits
• Truncus
• Cyanotic
• Eisenmenger

• Size makes a difference
  (ASD > 2 cm, VSD greater than 1 cm, PDA > 0.6-0.8 cm)
• Simple ASD
• Simple Aortic Disease
• Simple Mitral Disease
• Simple PDA
• Mild VPS

15%

severe

38%
mild

47%

moderate

• TOF
• SV Defects
• APV Drainage
• AVC
• Primum ASD
• Sub PS
• AoCo
• Ebstein
• VPS
• PR
• Complex PDA or VSD

Marelli A et al. *Am Heart J.* 2009
MODE OF DEATH IN ACHD

- Non-cardiac: 26%
- Perioperative: 17%
- Other cardiovascular: 18%
- CHF: 18%
- SD: 21%

Oeschlin. AJC, 2000
BURDEN OF HEART FAILURE IN ACHD

![Bar chart showing the trend of ACHD Heart Failure Hospitalizations from 1998 to 2005. The number of hospitalizations increases each year, with the highest in 2005.](attachment:chart.png)
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A 38 YEAR OLD MALE WITH COMPLEX SINGLE VENTRICLE

- A 38 year old male with complex single ventricle palliated with atrio-pulmonary Fontan
- Progressive CHF with multiple hospitalizations with acute decompensated CHF (4 hospitalizations in 6 months)
- Patient did not tolerate ACEI/Spironolactone (renal insuff) or carvedilol due to bradycardia with it
COMPLEX SINGLE VENTRICLE CASE - CONTINUED

- **CARDIOVASCULAR EXAM**
  - Cyanosis, Clubbing
  - JVP ~16cm no A,C,V waveforms
  - Healed scars of sternotomy
  - PMI in right chest
  - Single S1 and S2 (no TV or PV)
  - 3/6 Holosystolic murmur along lower sternal borders

- **MANAGEMENT**
  - Hospitalized
  - IV Diuresis
  - IV Milrinone
INVESTIGATIONS
LABS

- **BNP**: Elevated in several thousands
- **LFT**: Normal except for elevated GGT
- **Renal function**: Mildly elevated BUN, Normal creatinine
INVESTIGATIONS

- Pulmonary venous atrium
- Single ventricle
- Severe AV valve regurgitation
- Fontan Atrium
- Right pulmonary artery
- Left sided superior vena cava
- Massively dilated Left sided right atrium
WHAT IS THE BEST STEP TO PREVENT RECURRENT HEART FAILURE RELATED ADMISSIONS AND MORTALITY?

1. Medical management with ACE-I or Entresto, Carvedilol, spironolactone, diuretics +/- Digoxin
2. Mechanical AV valve replacement and Fontan conversion
3. Referral for heart and possibly liver transplant
4. Mechanical circulatory support
5. Referral for palliative care
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CAUSES OF CHF IN CONGENITAL HEART DISEASE

Volume Overload
Valve insufficiency / L→R shunts

Pressure Overload
Obstructive Lesions

Myocardial Dysfunction
Coronary anomaly, hx CP bypass

Pulmonary Hypertension

Heart Failure

Intractable Arrhythmias

Cyanosis
AHA CLASSIFICATION OF HEART FAILURE

At Risk for Heart Failure

STAGE A
At high risk for HF but without structural heart disease or symptoms of HF

e.g., Patients with:
- HTN
- Atherosclerotic disease
- DM
- Obesity
- Metabolic syndrome or Patients
- Using corticosteroids
- With history of cardiomyopathy

STAGE B
Structural heart disease but without signs or symptoms of HF

e.g., Patients with:
- Previous MI
- LV remodeling including LVM and new EF
- Asymptomatic valvular disease

Development of symptoms of HF

HFpEF

THERAPY

Goals
- Heart healthy lifestyle
- Prevent vascular, coronary disease
- Prevent LV structural abnormalities

Drugs
- ACEI or ARB as appropriate
- Beta blockers as appropriate
- In selected patients, ICD
- Resynchronization or valvular surgery as appropriate

Heart Failure

STAGE C
Structural heart disease with prior or current symptoms of HF

e.g., Patients with:
- Known structural heart disease and HF signs and symptoms

Refractory symptoms of HF at rest despite GDMT

HFREF

THERAPY

Goals
- Control symptoms
- Improve HRQOL
- Prevent hospitalization
- Prevent mortality

Drugs for routine use:
- Diuretics for fluid retention
- ACEI or ARB
- Beta blockers
- Aldosterone antagonists

Drugs for use in selected patients:
- Multi-target, beta blockers, digoxin
- ACEI and ARB
- Digitalis

In selected patients:
- CRT
- ICD
- Resynchronization or valvular surgery as appropriate

STAGE D
Refractory HF

e.g., Patients with:
- Marked HF symptoms at rest
- Recurrent hospitalizations despite GDMT

THERAPY

Goals
- Control symptoms
- Improve HRQOL
- Reduce hospital readmissions
- Establish patient’s and - of-life goals

Options
- Advanced care measures
- Heart transplant
- Chronic therapies
- Temporary or permanent MCS
- Experimental surgery or drugs
- Palliative care and hospice
- ICD deactivation
CONGESTIVE HEART FAILURE IN ADULT CONGENITAL HEART DISEASE

1. Adult Congenital Heart Disease & Long Term Issues
2. Case
3. Causes of Heart Failure in Congenital Heart Disease
4. Ventricles in Congenital Heart Disease
   a. Systemic ventricular dysfunction
      i. LV morphology
      ii. RV morphology
   b. Sub-pulmonary ventricular dysfunction
   c. Single ventricular dysfunction
5. Neurohormonal aspects and Biomarkers
6. Management approach
BORN TO BE BAD?!
3 VENTRICULAR PROBLEMS UNIQUE TO CHD

Cardiac Abnormality
Abnormal Musculature

TOF Sub-Pulmonary RV dysfunction

D-TGA Atrial switch Sub-Systemic RV dysfunction

Exercise impairment

CHF in ACHD

Neuro-hormonal Activation

Single ventricular dysfunction (HLHS)

Images: Boston Children’s Hospital
DIFFERENCES BETWEEN RV AND LV

**RV**
- Shape: Triangular
- Pumps to: low resistance circuit
- Fiber arrangement: 2 layers
- Single (Right) Coronary supply
- Single fascicle

**LV**
- Shape: Conical
- Pumps to: high resistance circuit
- Fiber arrangement: 3 layers
- Supplied by LAD and Circumflex
- Two fascicles
TETRALOGY OF FALLOT

SUB-PULMONARY RIGHT VENTRICULAR DYSFUNCTION
TETROLOGY OF FALLOT

- Patch to Enlarge Narrowed Pathway from RV to PA
- VSD Patch (To Close Opening Between Ventricles)
- Relief of pulmonary stenosis with patch
LVEF & RVEF IN TOF

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

\[ r = 0.58 \]

\[ p < 0.001 \]
D-TRANSPOSITION OF THE GREAT ARTERIES (D-TGA)- ATRIAL SWITCH OPERATION

SYSTEMIC RIGHT VENTRICULAR DYSFUNCTION
D-TGA, ATRIAL SWITCH OPERATION
MUSTARD OR SENNING OPERATIONS

Image: Boston Children's Hospital
CAUSES OF VENTRICULAR DYSFUNCTION
IN ATRIAL SWITCH PATIENTS

- Prevalence 8-48%

- Mechanisms:
  1. Myocardial Fiber arrangement
  2. Single Fascicle
  3. Ventricular interaction
  4. Ventricular dys-synchrony
  5. Impaired ventricular filling
  6. Single coronary supply

Kirjavainen, JTCTS 1999
Lange. Circulation 2006
Reich. Heart 1997
Milane T. JACC 2000
Chow P. AJC 2008
Tulveski I. AJC 2002
RV ANATOMY-FIBER ARRANGEMENT

A. Ao, PT, RV, LV
B. PT, RV, LV
C. PT, TV

Superficial Middle Deep

Ho. Heart 2006;92 i2-i13
HYPOPLASTIC LEFT HEART SYNDROME - FONTAN PALLIATION

SINGLE VENTRICULAR DYSFUNCTION
HYPOPLASTIC LEFT HEART SYNDROME
FONTAN OPERATION

Classic Atriopulmonary Fontan  Lateral Tunnel  External Conduit
REPAIR OF A SINGLE VENTRICLE

- **Fontan operation**
- **Principle:**
  - Use the single ventricle to pump blood to the body
  - Systemic venous blood (SVC & IVC) is allowed to flow passively to the lungs, without a pumping chamber
  - This is achieved in stages (SVC connected first) and final repair is called Fontan operation
- **May have poor cardiac output despite preserved ventricular function**
SINGLE VENTRICULAR PHYSIOLOGY IS A MULTISYSTEM DISEASE

High venous pressure leads to chronic passive liver congestion, which progresses to fibrosis and cirrhosis, with chronic ascites.

High venous pressure in the gut can lead to PLE.

Varicosities and venous stasis ulcers in the legs are common.

Plastic bronchitis due to elevated lymphatic pressure, may be fatal.

Proteinuria, renal insufficiency often develop with age.
1. Medical management with ACE-I or Entresto, Carvedilol, spironolactone, diuretics +/- Digoxin
2. Mechanical AV valve replacement and Fontan conversion
3. Referral for heart and possibly liver transplant
4. Mechanical circulatory support
5. Referral for palliative care
WHAT IS THE NEXT BEST STEP TO PREVENT HEART FAILURE AND RECURRENT ADMISSIONS?

1. Medical management with ACE-I or Entresto, Carvedilol, spironolactone, diuretics +/- Digoxin
2. Mechanical AV valve replacement and Fontan conversion
3. Referral for heart and possibly liver transplant
4. Mechanical circulatory support
5. Referral for palliative care
FONTAN CONVERSION AND MECHANICAL AV VALVE REPLACEMENT
Patient was discharged home and continues to do well 2 years post surgery.
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DISTRIBUTION OF PEAK VO₂ IN DIFFERENT DIAGNOSTIC GROUPS

- Aortic coarctation: 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

Diller G et al. Circulation. 2005
NEUROHORMONAL ACTIVATION IN ACHD

- N=53 (16 SV, 7 SRV, 20 TOF)
- NYHA II in majority
- Peak VO2 & VE/VCO2 slopes correlated with functional class

Bolger Circulation 2002
BNP AS A PROGNOSTIC MARKER IN ACHD

- 49 consecutive ACHD pts
- ~50% NYHA Class II
- Median follow-up: 8 years
- 36% TOF, 30% single V, 15% systemic RV

Giannakoulas Am J Cardiol 2010
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APPROACH TO ADVANCED HEART FAILURE IN CONGENITAL HEART DISEASE
If worsening symptoms, elevated biomarkers, exercise tolerance:
- Optimize medical management (drugs may be less effective)
- Consider hemodynamic evaluation
- Consider devices, surgical intervention, cath intervention, if needed (“fixable” lesions much more common)

If no improvement or no other interventions indicated:
- Consider transplant
- Consider mechanical circulatory support

If not a candidate:
- Referral to palliative care
HEART FAILURE TREATMENT IN ACHD

A) Heart failure treatment in acquired heart failure
- Neurohormonal modulation
  - RAAS inhibitors / β-adrenergic blockers / Aldosterone antagonists
- Invasive hemodynamics to guide treatment
- EP device therapy
  - ICD / CRT / Ablation
- Structural intervention

B) Heart failure treatment in ACHD
- Neurohormonal modulation
- EP device therapy
  - ICD / CRT / Ablation
- Structural intervention
- Invasive hemodynamics to guide treatment decisions

Ped Cardiol Dec 2013
LIMITED EVIDENCE IN ACHD

**Acquired HF**
- Large trials – thousands of pts
- Large number of events over short time interval
- Relatively homogeneous HF etiology
- Well studied prognostic markers

**HF in ACHD**
- Tiny trials – 10’s of patients
- Few events over decades
- Heterogeneous anatomy, physiology, surgical hx
- Few prognostic markers
- Standard HF Rx not studied in CHD population – **extrapolate with caution**
Management Considerations (Some Limited Data Exists)

- **Systemic LV failure** - reasonable to follow guidelines for acquired heart disease

- **Systemic RV failure**
  - **Valsartan** had no effect on event free survival, but improved EF in “symptomatic” pts
  - **Beta Blockers** - Several trials (Bisoprolol/Carvedilol) demonstrated possible benefits and may be considered
  - **Sildenafil** – meta analysis (612 pts) demonstrated improved hemodynamic parameters in HFrEF (but not HFpEF) vs. placebo. Well tolerated, but no improvement in QOL

- **CRT** – handful of studies in heterogeneous populations (systemic RV, single V, variable severity of HF, all ages), most showed some improvement in EF

*Circ 2013
In J Card 2014*
CRT indications in adults with congenital heart disease

- **Systemic LV**
  - LVEF ≤35%
    - Sinus rhythm
    - NYHA II-IV
    - LBBB
    - QRS ≥150 ms
      - Class I, Level B
  - LVEF >35%
    - Nyha I-IV
    - >40% V-pacing
      - Class IIa, Level B

- **Systemic RV**
  - RVEF ≤35%
    - RV dilation
      - NYHA II-IV
      - RBBB; QRS ≥150 ms
        - Class IIa, Level C
  - RVEF >35%
    - Nyha I-IV
    - >40% V-pacing
      - Class IIb, Level B

- **Single ventricle**
  - EF ≤35%
    - Ventricular dilation
      - NYHA II-IV
      - QRS ≥150 ms
        - Class IIa, Level C
  - EF >35%
    - Cardiac surgery
      - NYHA I-IV
      - Progressive ventricular dilation/dysfunction
        - Class IIb, Level B
    - TV surgery
      - NYHA I-IV
      - RBBB; QRS ≥150 ms
        - Class IIb, Level B

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Lifestyle

Daily sports participation improves event free survival in patients with systemic RV

Log Rank = 4.58; df = 1; p = 0.032

Int J Cardiol 2015
MECHANICAL SUPPORT IN ACHD
MECHANICAL CIRCULATORY SUPPORT IN UNIVENTRICULAR HEARTS

Seminars in Thor and Cardiovasc Surg 2015
IMPELLA ASSISTANCE IN CLASSIC FONTAN IN PIGS
IMPROVED HEMODYNAMICS

Circulation 2013
TRANSPLANT CONSIDERATIONS IN ACHD

- **Complex anatomy**
  - Heterotaxy or situs inversus and other systemic venous anomalies make anastomosis challenging, require baffles
  - Need to reconstruct pulm artery in Fontan patients
  - Atrial baffles in dTGA may be calcified resulting in difficult atrial anastomosis
  - May need increased length of donor SVC, innominate vein, or aorta
  - More complex surgery = longer ischemic time
  - AP collaterals or venovenous collaterals may complicate surgery, may be addressed before Tx

- **Isoimmunization**
  - Patients have often had multiple prior heart surgeries, homografts

- **Multiple prior thoracotomies**
  - Adhesions, more bleeding

- **Pulmonary hypertension**
  - more common
  - different pathogenesis than acquired HF
  - PVR harder to calculate in presence of shunts

- **Associated liver disease in Fontan patients**
  - guidelines lacking for prognosis, management

- **ACHD patients <3% of all heart transplants performed**
  - Higher early mortality, but better long term survival

- **Listing criteria developed for ischemic or dilated CM, associated with LV dysfunction**
  - ACHD patients less likely to meet 1A status, longer wait times
  - More difficult to support mechanically, less likely to get VAD support, so lower priority
UNIQUE ASPECTS OF CHF IN ACHD

- Growing population, younger than typical acquired HF
- Anatomy and morphology matter!
  - Systemic LV
  - Systemic RV
  - Sub-pulmonary (right) ventricle
  - Single ventricle – high risk of HF, particularly challenging
  - Some causes of HF are reversible
- Neurohormonal activation and Biomarkers are abnormal, as in acquired HF, but...
- Management approach differs
  - Medical therapy can’t simply be extrapolated from HF literature
  - Limited data available
  - Unique opportunities and challenges for surgical intervention, devices
- Transplant Challenges
  - Isoimmunization
  - Anatomy
  - Listing criteria
THANK YOU

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