Heart Failure in Patients with Adult Congenital Heart Disease

Damon M. Kwan, MD
Kaiser Permanente - SCPMG

Adult Congenital Heart Disease (ACHD): What are the numbers?

- Prevalence ~8/1000 live births (4/1000 to 50/1000)
  - US: between 8 and 10/1000 live births (data from CDC)
  - Europe: 6.9/1000 live births
  - Asia: 9.3/1000 live births
- Survival is increasing with advances in medical and surgical therapy
- Adults with CHD > children with CHD
  - 15% severe disease
  - 33% moderate disease
- Most have had "reparative"/"palliative" rather than "corrective" surgery

Disclosures: None
Heart Failure (HF) Hospitalizations in ACHD

- Increasing ACHD hospitalizations
    - Total – 102%
    - HF-related – 85%
- 2007 – Nationwide Inpatient Sample
  - 84,000 ACHD hospitalizations
  - 17,000 with diagnosis of HF
  - Overall mortality – 4.1%


Heart Failure

“complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill or eject blood”

“Traditional” Heart Failure in Adults

Left heart failure
- Myocardial ischemia
- Systemic hypertension
- Valvular heart disease
- Cardiomyopathies

Right heart failure
- Pulmonary arterial hypertension
- Valvular heart disease

Heart Failure in ACHD

Structural changes at birth:
- Pressure load
- Volume load
- Hypoplasia (“size”)

Cardiac Surgery:
- Timing and era of repair
- Myocardial preservation / pump time
- Scars (atriotomy / ventriculotomy)
- Coronary arteries
- Conduction system

Electrical:
- Dyssynchrony
- Chronic pacing

Genetics:
- Syndromes (e.g., Noonan’s)
- Left ventricular non-compaction

Heart Failure in ACHD

- Right heart failure
- Left heart failure
- Inadequate end-organ perfusion
  - Decreased SVR in the face of normal EF (end-stage liver disease / portal hypertension)

Clinical Presentation: Challenges

- Symptom reporting
  - Patients are unable to detect subtle changes in exercise capacity
  - Symptoms are underreported
  - At time of symptom recognition, extent of ventricular dysfunction and valve disease may be severe and irreversible
- Mechanism of HF is complex and individualized
Diagnosis of HF: Challenges

- “One size does not fit all”
- Based on anatomy
- Evaluate for:
  - Residual shunts
  - Baffle stenosis
  - Valvular / conduit dysfunction
  - Collateral vessels
**Diagnosis of HF: Modalities and Pitfalls**

- Echocardiogram
  - Right ventricular size and function (systolic / diastolic)
  - Hemodynamic evaluation
- Cardiac CT scan
- Cardiac MRI/A
- Cardiac catheterization
- Stress testing / cardiopulmonary exercise stress testing

---

**Diagnosis of HF: BNP**

- “Traditional” heart failure
  - Diagnosis / prognosis / therapeutic monitoring
- Wide range of values that reflect the heterogeneity of patients and pathophysiology
  - Volume / pressure overload
  - Cyanotic heart disease
- Correlations seen in ACHD:
  - Systemic ventricular dysfunction
  - Mortality
  - However, reference values are lacking

---

**HF in ACHD: Neurohormonal Activation**

---

**Diagnosis of HF: Role of BNP**

- For the integrated evaluation and monitoring of children with known heart disease, to allow the further defining of severity and progression of heart failure, and its response to therapy
- As an adjunctive marker, not a stand-alone test, in the screening of hemodynamically significant cardiovascular disease as well as in the prognosis of children undergoing cardiac surgery
HF Therapy in ACHD: Considerations
• Mechanistic differences in development of HF
• Heterogeneity in general and disease-specific ACHD populations
• Similar (but also not) to “traditional” HF patients
  – Functional impairment
  – Neurohormonal activation
  – Adverse cardiac remodeling
• No guideline-based therapy / limited data
  – Exclusion from large trials
  – Small underpowered retrospective studies

Heart Failure in ACHD
• Tetralogy of Fallot
• Transposition of the great arteries (systemic right ventricle)
  – D-transposition of the great arteries s/p atrial switch procedure
  – Physiologically / congenitally corrected transposition of the great arteries
• Single ventricle physiology / Fontan
• Pulmonary hypertension

Tetralogy of Fallot (ToF)
• Morphologic spectrum
  – VSD and overriding aorta with minimal pulmonary stenosis
  – Pulmonary obstruction is so severe (pulmonary atresia with VSD)
• Epidemiology:
  – Represents 10% of all congenital heart disease
  – >90% survival
  – 14% with NYHA class 2 or greater symptoms
• Heart failure mechanisms:
  – Right heart failure
    • Severe pulmonic regurgitation
    • Tricuspid regurgitation
    • RV diastolic dysfunction
  – Left heart failure
    • Ventricular-ventricular interaction
    • Elevated EDP
• Tetralogy of Fallot
  • Morphologic spectrum
    – VSD and overriding aorta with minimal pulmonary stenosis
    – Pulmonary obstruction is so severe (pulmonary atresia with VSD)
  • Epidemiology:
    – Represents 10% of all congenital heart disease
    – >90% survival
    – 14% with NYHA class 2 or greater symptoms
  • Heart failure mechanisms:
    – Right heart failure
      • Severe pulmonic regurgitation
      • Tricuspid regurgitation
      • RV diastolic dysfunction
  – Left heart failure
    • Ventricular-ventricular interaction
    • Elevated EDP
History of ToF Surgery

- Central shunt palliation
  - 1944 (Nov 29) – Blalock, Taussig, Thomas
  - 1946 – Potts
  - 1962 – Waterston
  - 1966 – Cooley

- “Early” complete repair (1950 to 1970)
  - 1954 – Lillehei – extracorporeal circulation
  - 1955 – Kirklin – “heart-lung machine” or cardiopulmonary bypass circuit

“Early” Complete Repair

- Patient characteristics/outcomes:
  - Mortality ~7-14% by early 1960s
  - Age – 15 months to 54 years
  - Central shunts – 43 to 70%

- Surgical technique:
  - Left heart was vented via the apex of the LV
  - Median sternotomy / RV ventriculotomy (longitudinal or transverse)
  - VSD closure (pericardial or prosthetic)
  - Division and/or resection of infundibular muscle bundles and relief of pulmonary valve stenosis
  - Infundibular patch (if resection of muscle not enough to enlarge RVOT)
  - Transannular patch (if pulmonary valve annulus was too small)

“Early” Recommendations

- Symptomatic disease (at any age) = surgical indication

- Age:
  - < 5 years of age
    - Shunting procedure initially followed by complete repair before age 20
    - Volume overload of the left ventricle
  - ≥ 5 years of age
    - Complete repair
    - Ideal age between age 9 and 12
    - Late repair – RV pressure overload (prolonged) – RV diastolic dysfunction

ToF Surgery: Modern Era (1970 - present)

- Shift toward earlier surgery in the neonatal period
  - Complete repair by age 6 months (no later than 12 months)

- Modifications:
  - VSD closure (patch) - primary closure resulted in heart block
  - Transatrial/transpulmonary approach - RV ventriculotomy resulted in chronic pulmonic regurgitation, worsening RV function, increased arrhythmias and sudden cardiac death
  - Routine and generous transannular patching has been abandoned
  - Maintain the integrity and competence of the pulmonary valve (even when this implies insertion of a bioprosthetic valve)
  - Avoidance of free pulmonary regurgitation, at the expense of residual mild to moderate pulmonary stenosis – generally accepted practice

ToF: “Corrective Surgery”

ToF: Adverse Post-op Consequences

- Transannular patch

RV to PA conduit
ToF: Post-op

Residua:
- RVOT &/or PA obstruction
- Atriotomy or ventriculotomy incision
- Muscular VSD
- Myocardial hypertrophy
- Chamber enlargement
- Aortic root dilatation
- Aortic regurgitation

Sequela:
- VSD patch leak
- RVOT scar/aneurysm
- Pulmonary regurgitation
- RV-PA valved conduits
- Conduction defects
- Aortic regurgitation

ToF: Myocardial Dysfunction

- Large pre-repair aortic-pulmonary shunt and LVVO
- Inadequate myocardial preservation
- Significant pulmonary regurgitation
- Large RVOT aneurysm/scar
- Significant aortic regurgitation
- Endocarditis and coronary embolization
- Superimposed degenerative aortic stenosis, HTN, or atherosclerotic CAD

HF in ToF: Management and “Prevention”

Heart failure mechanisms:
- Right heart failure
  - Severe pulmonic regurgitation
  - Tricuspid regurgitation
  - RV diastolic dysfunction
- Left heart failure
  - Ventricular-ventricular interaction
  - Elevated EDP

HF in ToF: Management and “Prevention”

Heart failure mechanisms:
- Neurohormonal modulatory therapy / RV function
  - No clear benefit
  - Beta-blockers
    - 32 patients NYHA class 1-2 showed no improvement in NYHA class or RV function (bisoprolol vs. placebo)
    - Use may be more appropriate for the management of arrhythmias
  - ACE inhibitors
    - 64 patients mod/severe PR showed no improvement in RVEF (Ramipril vs. placebo)
    - Improvement in biventricular long axis function
    - RV restrictive physiology – improvement in LV EF / reduction in LVESVI

HF in ToF: Management and “Prevention”

Percutaneous / surgical interventions
- Pulmonary valve replacement (surgical / percutaneous)
- Tricuspid valve repair / replacement

Timing of PVR
- Optimal timing is unclear
- Current indications:
  - Symptoms
    - RVEDVi > 130-150 mL/m²
  - RV/LV volume ratio 2:1
HF in ToF: “Prevention”
- “Corrective” surgery but with long-term sequelae / late complications
- Pitfalls in care:
  - Symptoms underreported
  - Lost to follow-up
- Evaluation at specialized ACHD centers:
  - Annual (clinical exam / history; ECG; echocardiogram; ambulatory ECG monitoring)
  - Role of stress testing
  - Role of cardiac MRI/CT

HF in ToF: Take Home Points
- ToF patients represent a wide morphologic spectrum and are part of a very heterogeneous population.
- What can be “prevented”? 
  - Progression to profound RV dysfunction / right-sided heart failure
  - Sudden cardiac death
- “Prevention” of HF should include:
  - Recognition that “corrective” surgery has its costs and close follow-up is indicated.
  - Follow-up should be done under the direct / indirect guidance of specialized ACHD centers.

Transposition of the Great Arteries (TGA)
- Morphologic right ventricle serves as the systemic ventricle
- Two conditions:
  - d-transposition of the great arteries (d-TGA) s/p atrial switch
  - Congenitally corrected transposition of the great arteries

D-Transposition of the Great Arteries
- Prevalence = 4.73/10000 live births
  - >90% now surviving to adulthood
- Surgical “correction”
  - Atrial switch procedure (Mustard / Senning)
    - Late 1960s to late 1980s / early 1990s
  - Arterial switch procedure (Jatene / Lecompte)
    - Early 1990s to present

Late Complications in Intra-atrial Baffles
- SA nodal injury
- SVC obstruction
- Baffle obstruction or leak
- Atrial arrhythmias
- Systemic AV (tricuspid) valve regurgitation
- Systemic ventricular dysfunction
- Pulmonary arterial hypertension
- Pulmonary venous obstruction
- LVOT obstruction
- VSD patch leak
- Conduction defects
Late Complications in Arterial Switch

- Pulmonary Artery Stenosis
- Neo-aortic Valve Regurgitation
- Neo-aortic Root Dilatation
- Coronary Artery Abnormalities


Pulmonary Artery Stenosis
Neo-aortic Valve Regurgitation
Neo-aortic Root Dilatation
Coronary Artery Abnormalities

Warnes CA Circulation 2006;114:2699-2709.

Congenitally Corrected Transposition of the Great Arteries


Systemic AV valve regurgitation
Systemic ventricular dysfunction
"Stiff" baffles – fixed stroke volumes
Sinus nodal dysfunction
Progressive AV block (1-2%/year)

HF in TGA: Management

Medication | Trial type | n | OR | RVED area | RV size | NYHA | QoL | VO2 | RVEF | RV size | NT-proBNP
--- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | ---
Coreg | Retrospective | 31 Rx d-TGA | 4±2 mo | No | No | No | No | No | No | No | No
Toprol XL | Retrospective | 31 Rx d-TGA | 4±2 mo | No | No | No | No | No | No | No | No
Ramipril | Randomized Placebo | 17 Rx d-TGA | 1 year | No | No | No | No | No | No | No | No
Losartan | Randomized Placebo | 17 Rx d-TGA | 1 year | No | No | No | No | No | No | No | No
Valsartan | Randomized Placebo | 17 Rx d-TGA | 1 year | No | No | No | No | No | No | No | No


HF in TGA: Surgical Management

- Systemic AV valve regurgitation
  - Mechanism
  - Repair / replacement
  - Should be done before systemic ventricular function declines

TGA: Heart Failure Mechanisms and Considerations

- Systemic right ventricle
  - Systemic AV valve regurgitation
  - Systemic ventricular dysfunction
- d-TGA s/p atrial switch procedure
  - "Stiff" baffles – fixed stroke volumes
  - Sinus nodal dysfunction
- Congenitally corrected transposition of the great arteries
  - Progressive AV block (1-2%/year)
HF in TGA: Take Home Points

- TGA patients (d-TGA atrial switch / ccTGA) are at risk for systemic morphologic right ventricular dysfunction.
- What can be "prevented"?
  - Early intervention for systemic AV valve regurgitation
  - Sudden cardiac death
  - Options unfortunately are limited
- "Prevention" of HF should include:
  - Close follow-up should be done under the direct guidance of specialized ACHD centers.

The Fontan Patient

Fontan Procedure
(Single Ventricular Palliation)

Fontan Variants

Fontan Variants: Present Day

The Fontan Circuit
The Fontan Circuit

- Systemic venous blood is separated from pulmonary venous blood
- SVC and IVC are diverted into the pulmonary artery
  - Flow driven by difference between central venous and left atrial pressures
- Shunts are eliminated along with volume overload
- Resistances are no longer in parallel but rather in series (pressure overload)


The Fontan Circuit

- High risk for heart failure:
  - Ventricular remodeling and dysfunction
    - Right ventricle as the systemic ventricle
    - History of ventriculotomy during staged palliation
    - Chronic hypoxemia and ventricular volume loading (in childhood as part of staged palliation)
  - Chronic venous congestion
  - Cyanosis
- Mechanisms:
  - High afterload
  - Stroke work
  - Adverse ventricular-arterial coupling

The Failing Fontan

Palliation Not Cure: Costs of a Fontan Procedure

- Venous return is passive (no pump)
- Central venous pressure is increased
- Ventricular filling is limited – lower stroke volume (left-sided)
- Increased systemic vascular resistance
- Ventricle has to pump against increased SVR, mechanical impedance of Fontan pathway, and pulmonary vascular system
- Reduced cardiac output
- Perfusion profile is altered
- Increased inflammation

HF in Fontan Patients: Challenges in Medical Therapy

- Afterload reduction
  - Mechanistically makes sense – but speculative
  - May be detrimental in low SVR states (hepatic dysfunction)
- Pulmonary vasodilators
  - Low PVR is desirable / necessary given the lack of a subpulmonic ventricle
  - Measurement of PVR – technically difficult
- Diuretics
  - Treatment of venous congestion

Cirrhosis in the Fontan Patient

HF in Fontan Patients: Challenges in Medical Therapy

The Falling Fontan: Catheter Based Therapy
The Fontan Patient: Take Home Points

- The Fontan procedure is a PALLIATIVE procedure.
- Multidisciplinary care should be delivered at specialized ACHD centers.
- Heart failure can results from:
  - Ventricular dysfunction
  - Venous congestion
  - Cyanosis
  - “Failing” Fontan

Cardiac Transplantation in ACHD

- Listing for transplantation is not done so timely
  - Lack of risk models for transplant-free survival
  - “Atypical” exercise performance parameters for transplant listing
- CHD patients are typically listed at lower urgency
  - Higher rate of complications once listed
  - Lower utilization of mechanical circulatory support (7.7% compared with >19%)

Cardiac Transplantation in ACHD: Outcomes

HF in ACHD: Take Home Points

- Adults with ACHD is a growing population that is surviving longer and many will have heart failure.
- Heart failure in ACHD is comprised of a “non-traditional” and heterogeneous patient population.
  - Mechanism is complex and individualized.
  - Not one patient’s lesion is the same as the next.
  - Traditional HF therapies do not necessarily apply or work.
- However, there is a potential to “prevent” and therapy can be individualized.
Thank you for your attention.