Heart failure in adults with congenital heart disease -
Diagnostic and therapeutic strategies

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Definition Heart Failure

- In physiologic terms, HF is a syndrome characterized by either or both pulmonary and systemic venous congestion and/or inadequate peripheral oxygen delivery, at rest or during stress, caused by cardiac dysfunction

### General information

- The incidence of CHD ranges between 3-20 per 1000 live births.  
  Van der Bom T et al. Nat Rev Cardiol 2011;8:50-60

- Survival of newborns with complex CHD now approaches 90%, and 96% of newborns with CHD who survive their first year of life remain alive at 16 years of age.  

- > 1 million adults with CHD in the USA and > 1.2 million in Europe.

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### General information HF

- Few cardiac defects are corrected by surgery or catheter intervention

- Residual lesions are frequent and may cause symptoms – HF

- The prevalence of HF in children with CHD is not known
  - About 5% develop HF in childhood; 10-20% after Fontan operation
  - The prevalence of HF in adults after Fontan is nearly 50%

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Treatment of ACHD

- The combined effort of all faculties involved in the treatment of patients with CHD significantly improved the early outcome, however, late mortality remains relatively unchanged.

Death Hazard in ACHD

Heart failure = the new threat

Oechslin et al. Am J Cardiol 2000
Engelings C et al. 2016 IJC;211:31-36

Verheugt CL et al. Mortality in adult congenital heart disease. EHJ 2010;31:1220-29
To treat = to understand HF in CHD pathophysiology

<table>
<thead>
<tr>
<th>Adult Cardiology</th>
<th>Congenital heart disease</th>
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<tbody>
<tr>
<td>Impaired systolic function</td>
<td>Impaired systolic function</td>
</tr>
<tr>
<td>- Systemic left ventricle</td>
<td>- Systemic left ventricle</td>
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<tr>
<td>- Subpulmonary right ventricle</td>
<td>- Subpulmonary right ventricle</td>
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<tr>
<td>- Systemic right ventricle</td>
<td>- Systemic single ventricle</td>
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<tr>
<td>- Cyanotic systemic and subpulmonary ventricle</td>
<td>- Cyanotic systemic and subpulmonary ventricle</td>
</tr>
<tr>
<td>Preserved systolic function</td>
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<td>- Systemic left ventricle</td>
<td>- Systemic left and right ventricle</td>
</tr>
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<td></td>
<td>- Subpulmonary ventricle</td>
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Courtesy W. Budts

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Do not forget co-morbidities!

- Renal failure: 30-50% of CHD
- Blood disorders: central cyanosis
- Liver disease: Fontan; Ebstein malformation
- Protein loosing enteropathy: Fontan
- Plastic bronchitis: Fontan


First step of treatment = HF detection

Budts et al. Eur Heart J 2016
Asymptomatic, but clinical heart failure
-22.2% in Mustard repair for dTGA
-32.3% in ccTGA
-40.0% in Fontan palliation
Establish or confirm the underlying CHD diagnosis
- Identify concomitant/residual lesions and sequelae
- Assess ventricular function (sub-aortic & sub-pulmonary)
- Monitor disease progression
- Detect new & acquired lesions
- Guide further interventions

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**Figure 1** Diagnosis–treatment algorithm. CPET, cardiopulmonary exercise test; PVO₂, peak oxygen consumption; LV, left ventricle; RV, right ventricle. *Two-fold increase of baseline natriuretic peptide value within 6 months. **≥ 25% decrease of peak oxygen consumption.
Diagnostic tools beyond imaging

Biomarkers – natriuretic peptide

Excercise capacity


Medical treatment in CHD HF

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Medical treatment in CHD HF

Impaired systemic LEFT ventricle; EF < 40%
Asymptomatic or symptomatic
Increased neuro-hormonal and cardiac autonomic activity*

- RAAS blockers
- Bêta-blockers
- Mineralocorticoid receptor antagonists
- Diuretics (loop and thiazide)
- Digoxin

Extra benefits
- Rhythm control
- Blood pressure control
- Symptom control

*Ohuchi et al. Circulation 2003; Buchhorn et al. Cardiol Young 2003

Medical treatment in CHD HF

Impaired systemic RIGHT ventricle; EF < 40%
Asymptomatic
Not always increasing neuro-hormonal and cardiac autonomic activity

No medical therapy indicated

Extra benefits of RAAS* or bêta-blockers**
- Exercise duration
- AV valve regurgitation
- RV remodeling

Impaired sub-pulmonary LEFT or RIGHT ventricle; EF < 40%

Asymptomatic, stable biomarkers and stable exercise capacity

No medical therapy indicated

Pitfall*
- Impaired systemic left ventricular function in one third of the TOF patients!!

*Broberg et al. Am J Cardiol 2011
Medical treatment in CHD HF

Symptomatic, unstable biomarkers and stable exercise capacity

Impaired sub-pulmonary LEFT or RIGHT ventricle; EF < 40%

Bèta-blockers (bisoprolol)*
- Increase in BNP
- ACE-inhibitor (ramipril)**
- Improvement LV function

Diuretics (loop and thiazide)
Mineralocorticoid receptor antagonists
Pulmonary vasodilators (PAH)

Medical therapy in single ventricle and Fontan circulation
A suggestion

<table>
<thead>
<tr>
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<th>Asymptomatic</th>
<th>Symptomatic</th>
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</table>
| **Impaired LV function** | RAAS blockers
Bèta-blockers
Mineralocorticoid receptor antagonists
Digoxin                   | RAAS blockers
Bèta-blockers
Mineralocorticoid receptor antagonists
Diuretics (loop and thiazide)
Digoxin                    |

**Impaired RV function**

- **Stable BM, CPET**
  - No medication

- **Un-stable BM, CPET**
  - RAAS blockers
Bèta-blockers
Mineralocorticoid receptor antagonists
Digoxin

  - RAAS blockers
Bèta-blockers
Mineralocorticoid receptor antagonists
Diuretics (loop and thiazide)
Digoxin


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A) Normal (serial) biventricular circulation

B) univentrikulär (paralel) circulation

C) Fontan Circulation


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Medical R/ in single ventricle and Fontan circulation: a suggestion

Budts et al. Eur Heart J 2016

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- ACE inhibitors (enalapril) = no effect on exercise capacity
- Enalapril = no effect on ventr size, HF class, BNP, EF, or death/transplant
- Enalapril = no effect on Rs, cardiac output, diast. Function, exercise capacity
- Bêta-blockers (carvedilol) = effect on HF signs and symptoms
- Spironolactone = effect on PLE, endothelial function
- Diuretics = relief of symptoms
- Phosphodiesterase inhibitors and endothelin receptor antagonists = improves ventricular filling and myocardial function

• It is not known whether pharmacological RAAS inhibition or adrenergic blockade produces similar effects in pts with a single LV vs RV. Stout 2016 Circ, Hsu 2010 Circ, Koide 1999 Am J Physiol
• There is some evidence that RAAS activation is not the dominant pathophysiological contributor to HF in patients with SV Dore 2005 Circ
• There may be differences in the effect of β-blocker therapy in SV patients depending on their age. Shaddy 2007 JAMA
• Ventricular preload is chronically reduced in Fontan circulation. Eicken 2008 IJC

Use of other ‘drugs’?

• Ivabradine
• Entresto (Sacubitril-Valsartan)
• Hydralazine, isosorbide dinitrate
• Iron substitution
• B_{12} substitution – acid folate substitution
• Antiplatelets therapy – oral anticoagulation


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From drugs to device therapy

• Cardiac resynchronization therapy
  – Improvement of functional class
  – Better response of systemic LV than in systemic RV
  – Best CRT response in patients under continuous RV pacing
  – Patients with single ventricle physiology benefit from optimized pacing sites


Beyond pills and devices…

Cardiac Rehabilitation

- Management of regular follow-up
- Treatment adherence
- Educational interventions on health behavior
- Filling knowledge gaps
- Interfere with patient’s psychological condition

• Heart failure in CHD is an expanding problem
• Prevention by structural optimization is probably the best treatment
• Limited or no data are available to treat CHD HF patients with evidence level A
• Experience based medicine is the only backbone for the treatment of the current CHD patients
• CHD community must try to establish randomized controlled trials to increase evidence

Thank you!