

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



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- 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



Heart failure Society of America. Executive summary: HFSA 2006 comprehensive heart failure practice guideline. J Card Failure 2006;12:10-38

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 Deutsches Herzzentrum München **General information** Technische Universität München 

- 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.
Wren C et al. Heart 2001;85:438-43
- > 1 million adults with CHD in the USA and > 1.2 million in Europe.

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 Deutsches Herzzentrum München **General information HF** Technische Universität München 

- 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

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- 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.

| Altersgruppen | Gestorbene 1990 | Gestorbene 2013 |
|---------------|-----------------|-----------------|
| < 1 | 777 | 226 |
| 1 - < 15 | 153 | 38 |
| 15 - < 45 | 116 | 86 |
| 45 - < 65 | 75 | 50 |
| 65 - < 75 | 31 | 31 |
| > 75 | 62 | 60 |
| gesamt | 777 | 491 |

Abbildung auf Grundlage von Daten des Deutschen Herzzentrums

Abb. 7114. Todesfälle bei angeborenen Fehlbildungen des Kreislaufsystems (ICD-10 Q20-Q28) von 1990 auf 2014

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Death Hazard in ACHD

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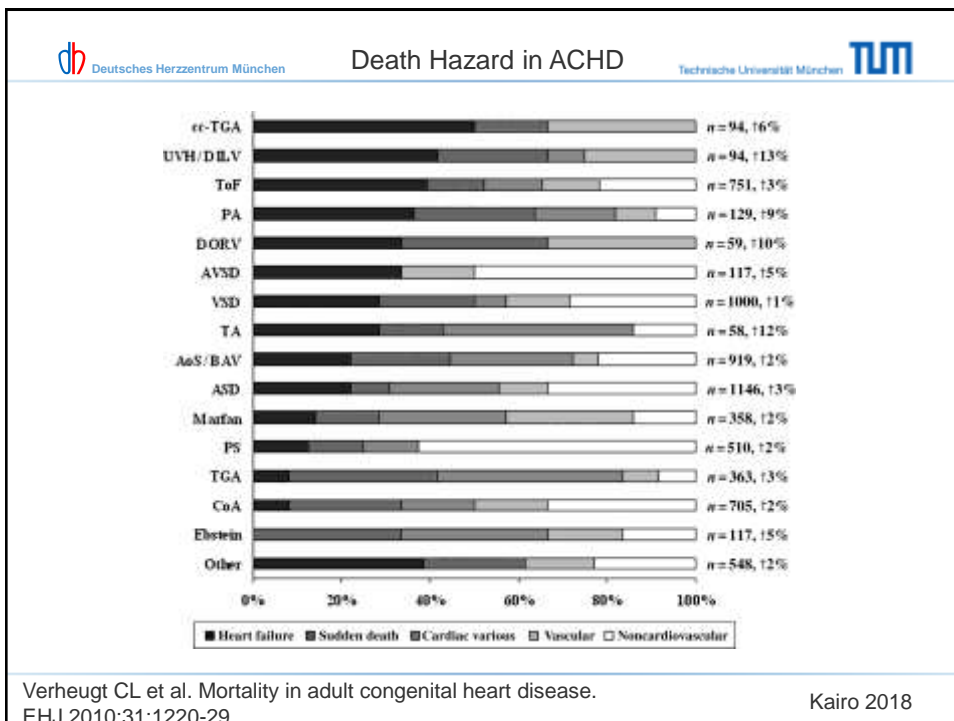
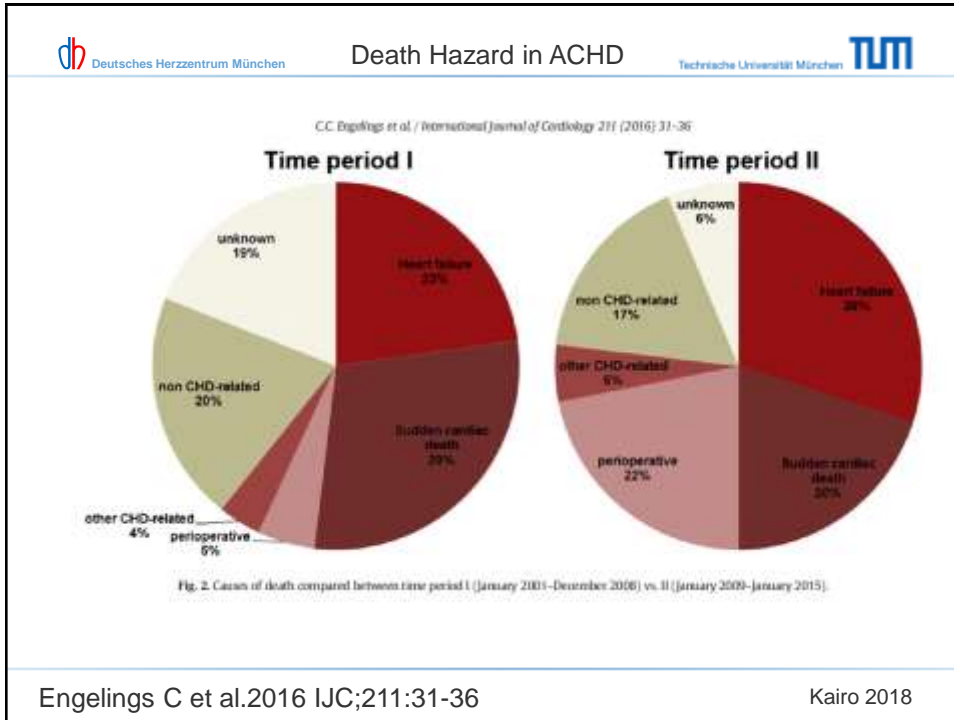
Heart failure = the new threat

| Mechanism | Count | Percentage |
|----------------------|-------|------------|
| CHF | 41 | 21% |
| SD | 51 | 26% |
| Other cardiovascular | 36 | 18% |
| Perioperative | 36 | 18% |
| Non-cardiac | 33 | 17% |

| CHD | SD | CHF | Perioperative | Non-cardiac | Other cardiovascular |
|--------------------------------|----|-----|---------------|-------------|----------------------|
| Atrioventricular septal defect | 15 | 0 | 0 | 0 | 0 |
| Patent ductus arteriosus | 4 | 0 | 0 | 0 | 0 |
| Univentricular connection | 25 | 0 | 0 | 0 | 0 |
| Complete transposition | 12 | 0 | 0 | 0 | 0 |
| Atrial septal defect | 23 | 0 | 0 | 0 | 0 |
| Ventricular septal defect | 30 | 0 | 0 | 0 | 0 |
| Tricuspid atresia | 12 | 0 | 0 | 0 | 0 |
| Tetralogy | 25 | 0 | 0 | 0 | 0 |
| Aortic valve anomaly | 9 | 0 | 0 | 0 | 0 |
| Cong. corrected transposition | 15 | 0 | 0 | 0 | 0 |
| Ebstein anomaly | 6 | 0 | 0 | 0 | 0 |
| Aortic coarctation | 4 | 0 | 0 | 0 | 0 |

FIGURE 1. Mechanism of death of the 197 deceased patients with adequate information to determine circumstances of their death. CHF = death due to chronic, progressive heart failure; Other cardiovascular = nonsudden death secondary to arrhythmia, endocarditis, and other cardiovascular causes; Perioperative = death within 30 days after cardiac surgery; SD = sudden death.

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To treat = to understand HF in CHD pathophysiology

| Adult Cardiology | Congenital heart disease |
|--------------------------------|--|
| Impaired systolic function | Impaired systolic function |
| - Systemic left ventricle | - Systemic left ventricle |
| - Subpulmonary right ventricle | - Subpulmonary right ventricle |
| | - Systemic right ventricle |
| | - Systemic single ventricle |
| | - Cyanotic systemic and subpulmonary ventricle |
| Preserved systolic function | Preserved systolic function |
| - Systemic left ventricle | - Systemic left and right ventricle |
| | - Subpulmonary ventricle |

Courtesy W.Budts
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| Adult Cardiology | Congenital heart disease |
|-----------------------|--------------------------|
| Impaired systolic fu | ction |
| - Systemic left venti | icle |
| - Subpulmonary rigl | it ventricle |
| | tricle |
| | ntricle |
| | and subpulmonary |
| Preserved systolic f | unction |
| - Systemic left venti | ight ventricle |
| | - Subpulmonary ventricle |

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 losing enteropathy: Fontan
- Plastic bronchitis: Fontan

Jensen et al. Int J Cardiol 2013; Lindsay et al. Am J Cardiol 2015;
 Pundi et al. J Am Coll Cardiol 2015; Schumacher et al. J Pediatr 2015; Saikin et al. Heart Vessels 2015

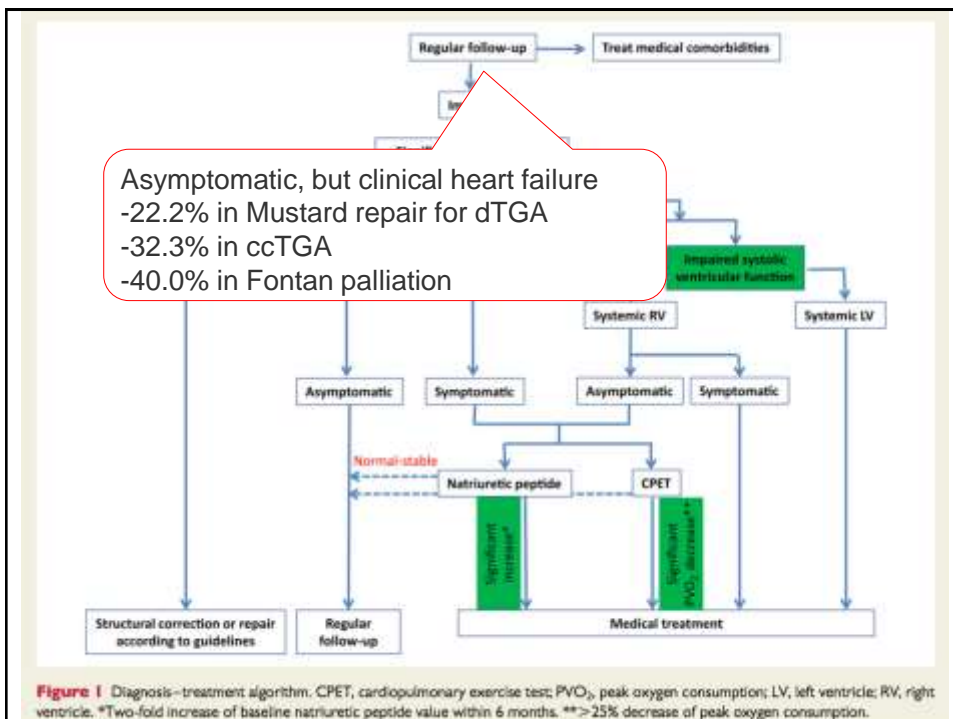
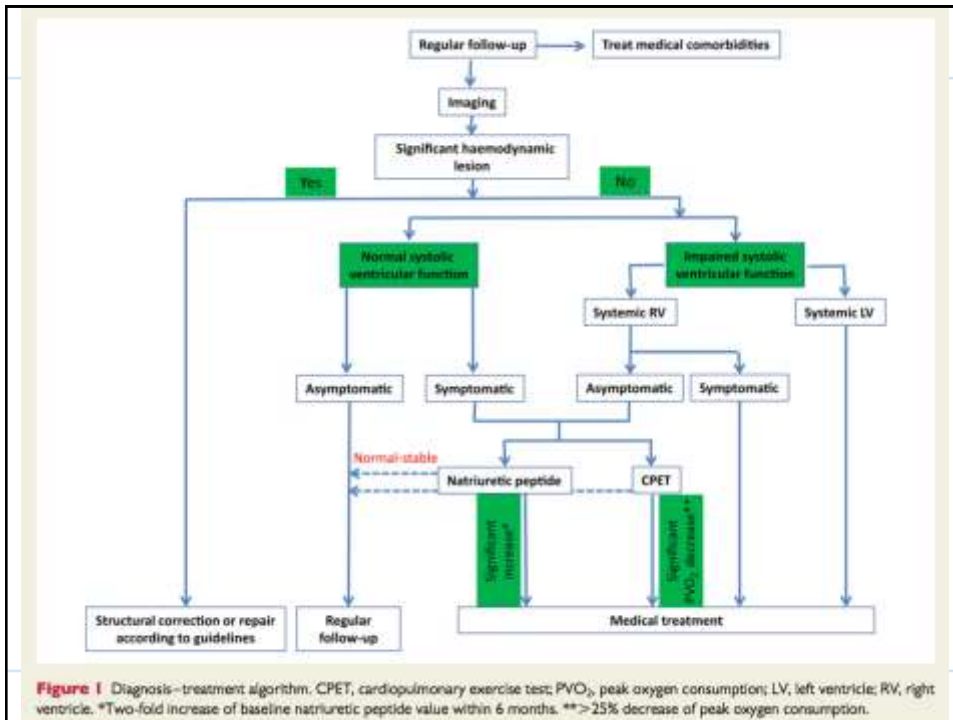
Courtesy W.Budts Kairo 2018

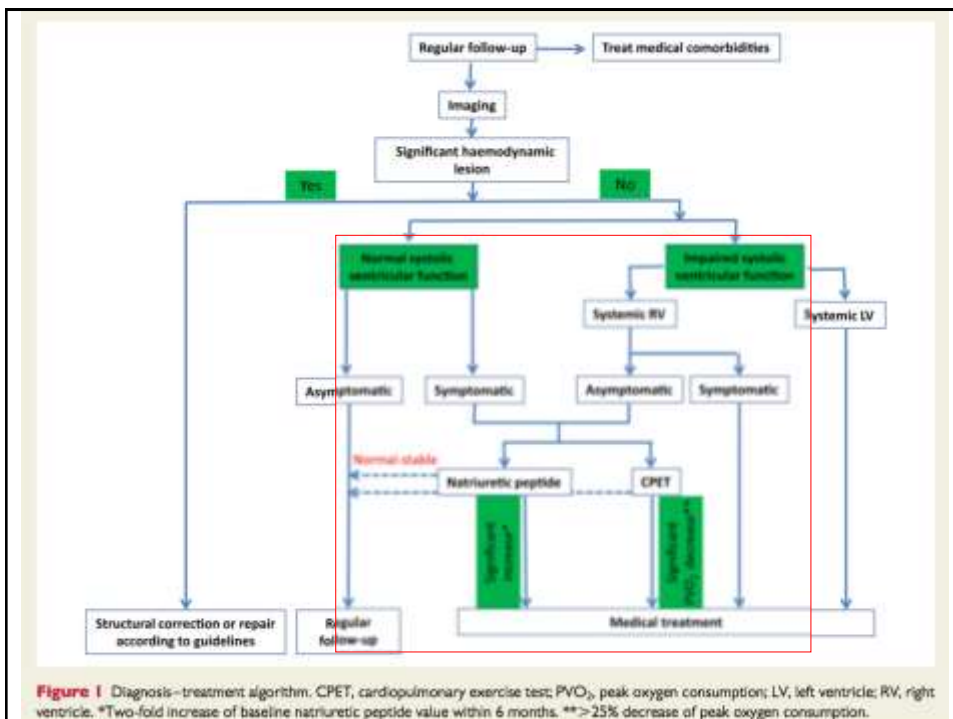
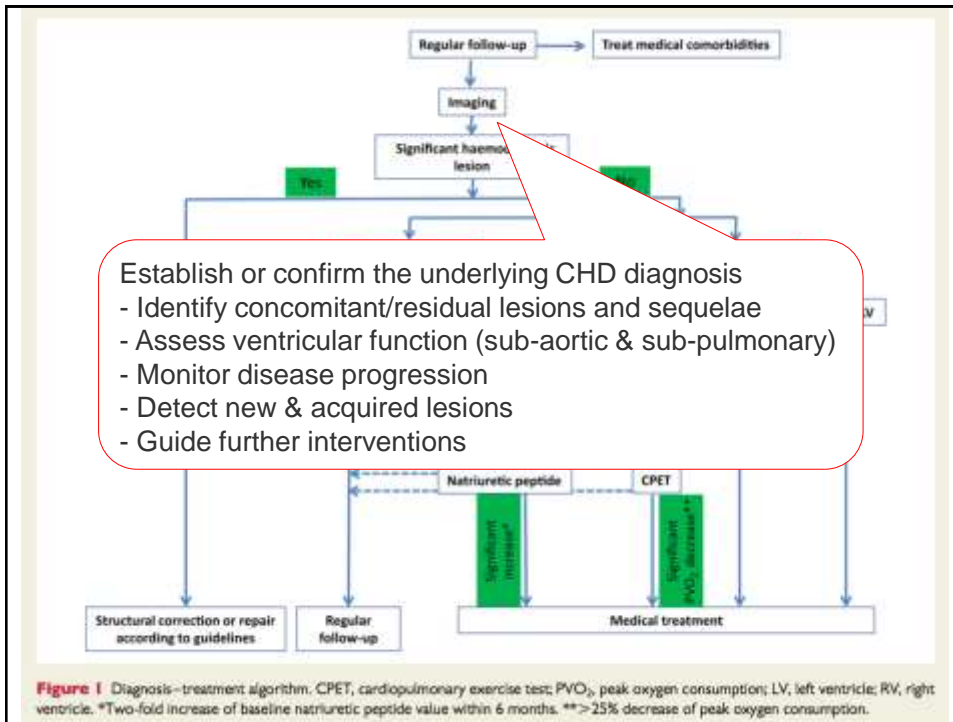




First step of treatment = HF detection


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.

Budts et al. Eur Heart J 2016 Kairo 2018





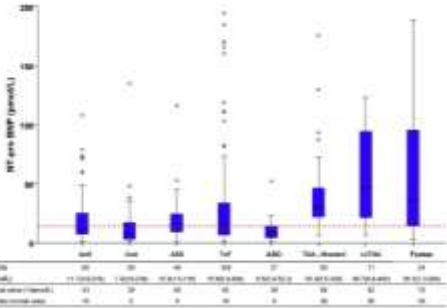




Diagnostic tools beyond imaging

Courtesy W.Budts

Biomarkers – natriuretic peptide

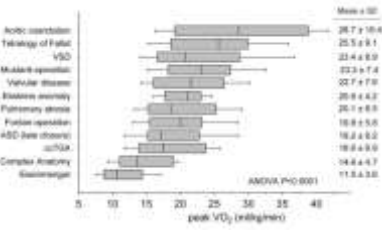


| Diagnosis | n | Median (IQR) | Percentage Normal (≤100) | Percentage Elevated (>100) |
|------------|----|--------------|--------------------------|----------------------------|
| MI | 11 | 10 (5-15) | 91 | 9 |
| CAD | 13 | 15 (10-20) | 69 | 31 |
| AFib | 10 | 20 (15-25) | 60 | 40 |
| HF | 10 | 30 (20-40) | 30 | 70 |
| ASD | 11 | 40 (30-50) | 27 | 73 |
| TGA | 10 | 50 (40-60) | 10 | 90 |
| ASD + TGA | 11 | 60 (50-70) | 9 | 91 |
| ASD + AFib | 11 | 70 (60-80) | 0 | 100 |
| Pulm | 11 | 90 (80-100) | 0 | 100 |

Figure 2. NT-pro-BNP levels by Type of Congestive Heart Disease

In a series of 86 patients (aged 65.4±12.8 years) with 40 different cardiac diagnoses, the best diagnosis, the percentage of patients with NT-pro-BNP levels above the reference value of 100 pmol/L is presented. Furthermore, the percentage of patients with NT-pro-BNP 3 times the reference value of 300 pmol/L is shown. MI = acute anterior MI; CAD = coronary artery disease; AFib = atrial fibrillation; HF = congestive heart failure; TGA = transposition of the great vessels; ASD = atrial septal defect; ASD + TGA = atrial septal defect + transposition of the great vessels; ASD + AFib = atrial septal defect + atrial fibrillation.


Exercise capacity




| Diagnosis | Mean ± SD |
|------------------------|-------------|
| Aortic coarctation | 28.7 ± 10.4 |
| Tetralogy of Fallot | 25.5 ± 9.1 |
| VSD | 22.4 ± 8.9 |
| Mitral stenosis | 22.3 ± 7.4 |
| Valvular disease | 22.7 ± 7.8 |
| Aortic stenosis | 20.8 ± 4.2 |
| Pulmonary stenosis | 20.1 ± 8.5 |
| Pulmonic regurgitation | 18.8 ± 5.5 |
| ASD (non-obstructive) | 18.2 ± 8.2 |
| ASD | 18.0 ± 9.0 |
| Complex Anatomy | 14.4 ± 4.7 |
| ASD | 11.5 ± 3.8 |

Figure 3. Distribution of peak V̇O₂ (mean ± SD) in different diagnostic groups. ASD = atrial septal defect; ASD (non-obstructive) = ASD without congenitally associated TGA; VSD = ventricular septal defect.

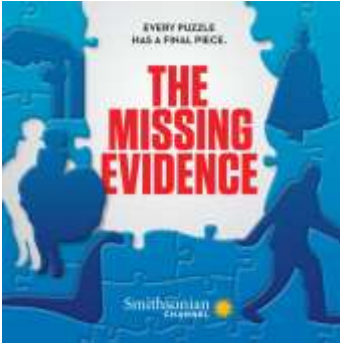
Eindhoven et al. J Am Coll Cardiol 2013; Diller et al. Circulation 2005
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Medical treatment in CHD HF

Courtesy W.Budts

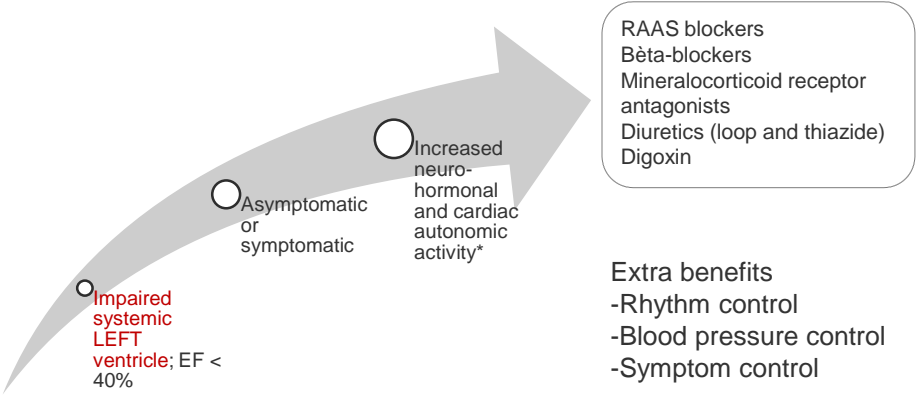


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Medical treatment in CHD HF

Courtesy W.Budts



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

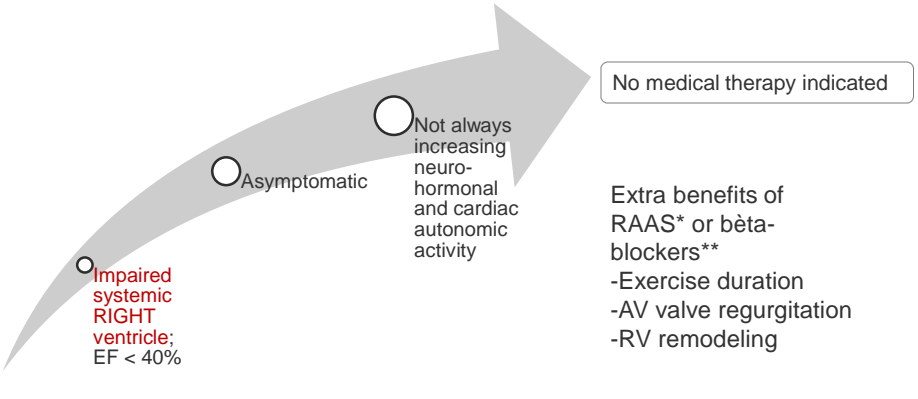
*Ohuchi et al. Circulation 2003; Buchhorn et al. Cardiol Young 2003

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Medical treatment in CHD HF

Courtesy W.Budts



Impaired systemic RIGHT ventricle; EF < 40%

Asymptomatic

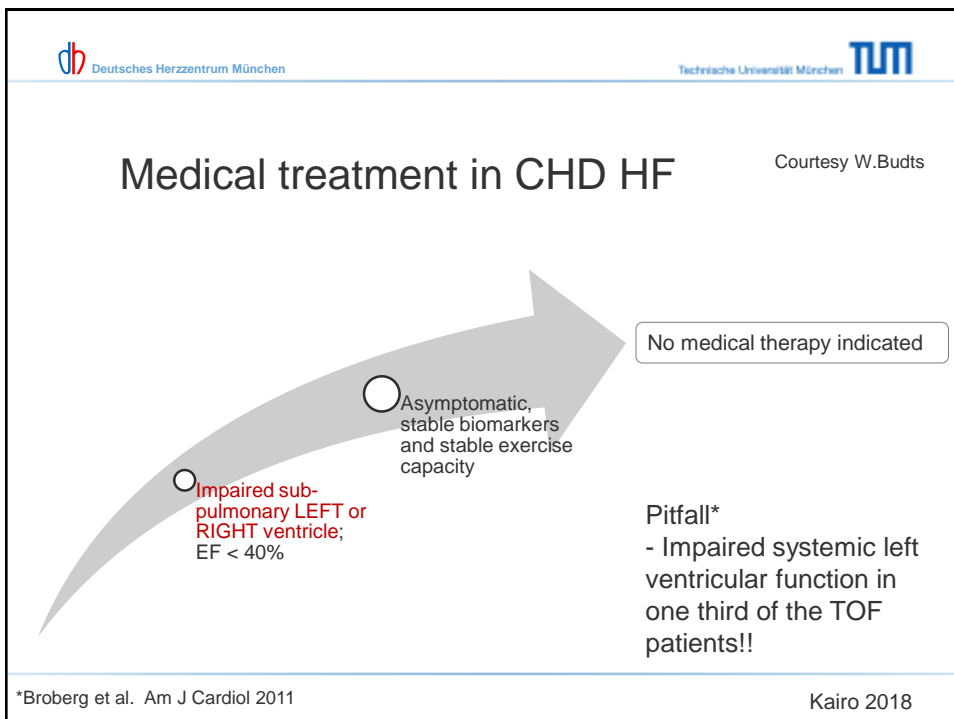
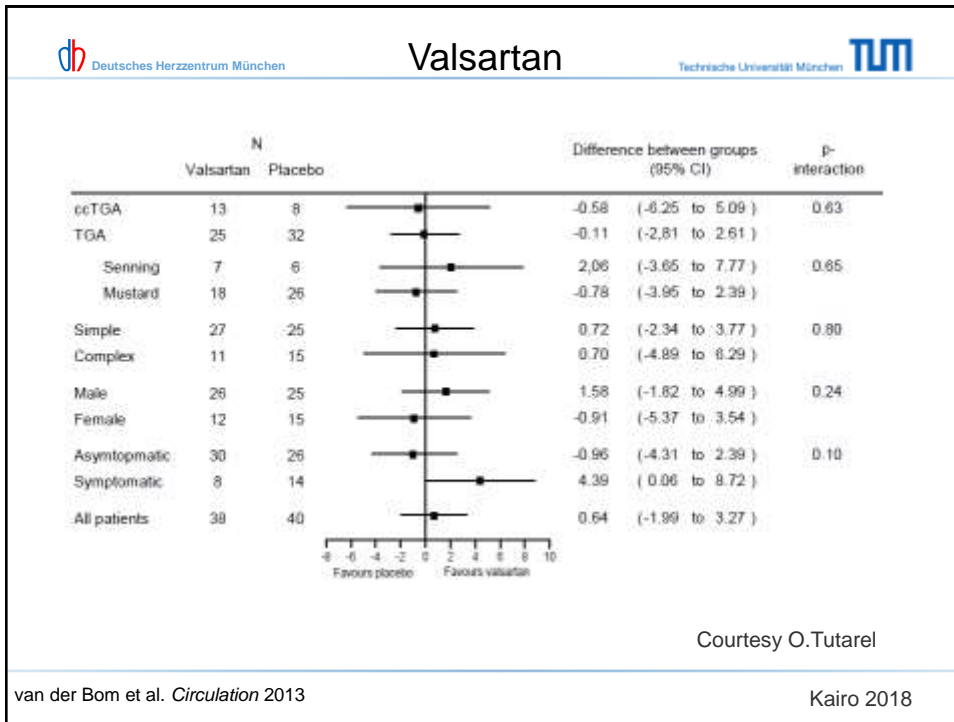
Not always increasing neuro-hormonal and cardiac autonomic activity

No medical therapy indicated

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

*Van der Bom et al. Circulation 2013; **Doughan et al. Am J Cardiol 2007

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Medical treatment in CHD HF

Courtesy W.Budts

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

Symptomatic, unstable biomarkers and stable exercise capacity

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

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

*Norozi et al. Caridiol Young 2007; **Babu-Narayan et al. Int J Cardiol 2012 Kairo 2018

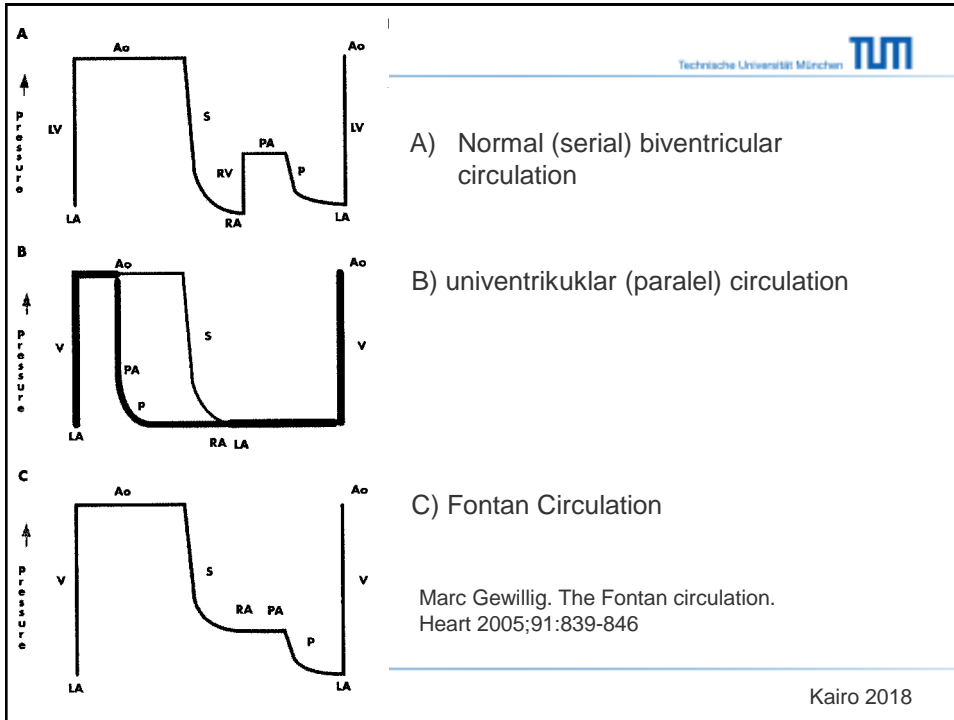
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Medical therapy in single ventricle and Fontan circulation

A suggestion

| | Asymptomatic | Symptomatic |
|-----------------------------|---|--|
| <i>Impaired LV function</i> | | |
| | RAAS blockers Bèta-blockers Mineralocorticoid receptor antagonists Digoxin | RAAS blockers Bèta-blockers Mineralocorticoid receptor antagonists Diuretics (loop and thiazide) Digoxin |
| <i>Impaired RV function</i> | | |
| - Stable BM, CPET | No medication | RAAS blockers Bèta-blockers Mineralocorticoid receptor antagonists Diuretics (loop and thiazide) Digoxin |
| - Un-stable BM, CPET | RAAS blockers Bèta-blockers Mineralocorticoid receptor antagonists Digoxin | RAAS blockers Bèta-blockers Mineralocorticoid receptor antagonists Diuretics (loop and thiazide) Digoxin |

Budts et al. Eur Heart J 2016 Kairo 2018



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

Budts et al. Eur Heart J 2016

- 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
- Bèta-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



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

Kouatli Circ 1997; Hsu 2010 Circ, von der Muhl 2004 ijc, Ishibashi Circ J 2011; Ringel Am J Cardiol 2003; Van De Bruaene Circ Cardiovasc Imaging 2014, Goldberg 2011 Circ; Hebert Circ 2014 Tempo


HF in SV patient


- 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



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Use of other 'drugs'?


- Ivabradine
- Entresto (Sacubitril/Valsartan)
- Hydralazine, isosorbide dinitrate
- Iron substitution
- B₁₂ substitution – acid folate substitution
- Antiplatelets therapy – oral anticoagulation

?

ESC Guidelines HF Eur Heart J 2016; Jankowska et al. Eur Heart J 2014; Courtesy W.Budts van der Wal et al. Heart 2015; de Boer et al. Thromb Res 2005
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From drugs to device therapy

Courtesy W.Budts

- 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


Janousek et al. Heart 2009; Khairy P et al. Int J Cardiol 2006;
 Cecchin et al. J Cardiovasc Electrophysiol 2009
 Kairo 2018

Beyond pills and devices...

Courtesy W.Budts

Cardiac Rehabilitation



Benefits of regular exercise:

- ↑ VO₂ max
- ↓ Resting HR
- ↑ Stroke volume
- ↑ Cardiac output
- ↑ Endothelial function
- ↑ Insulin sensitivity
- ↑ HDL cholesterol
- ↓ Blood pressure
- ↓ Risk of atherosclerosis
- ↓ Risk of stroke
- ↓ Risk of heart failure
- ↓ Risk of mortality

Potential risks of sedentary lifestyle:

- ↑ Risk of SCD, especially in non-athletes

Risk factors for exercise-induced SCD in CHD include:


- ↑ Age
- ↑ Disease complexity
- Ventricular dysfunction
- Pre-excitation
- Pulmonary hypertension
- Coronary artery disease
- Aortic disease
- Non-athletic athlete

Overall, long-term benefits generally prevail. Up to 70-80% reduction in age-adjusted mortality rate.


ACHD Nurse practitioner

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

Diller & Baumgartner Eur Heart J 2016;
 Moons et al. Eur J Cardiovasc Nurs 2002
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Conclusion

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- 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

Courtesy W.BudtsKairo 2018

