

CPET in Congenital Heart Disease

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Head of Exercise Laboratory

Board Member of CPX International



disclosures

institutional

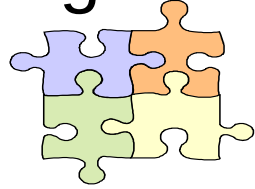
contribution to studies (Actelion, Medtronic, Edwards, Occlutech, Novartis, Lilly, Bayer, Bristol-Myers Squibb)
unrestricted grants (Pfizer, GlaxoSmithKline, Abbott, Actelion, Medtronic)

private

travel reimbursement (Actelion, Pfizer, GlaxoSmithKline, Lilly, OMT)
speakers reimbursement (Encysive, Pfizer, Actelion, Medtronic, Schiller, GlaxoSmithKline, OMT, AOP Orphan, Janssen)
writing reimbursement (Actelion)
consulting reimbursement (Actelion, Bayer, Ethypharm, GlaxoSmithKline)
shareholder (Pfizer)

CPET Indications

Diagnosis



Evaluation



Prognosis

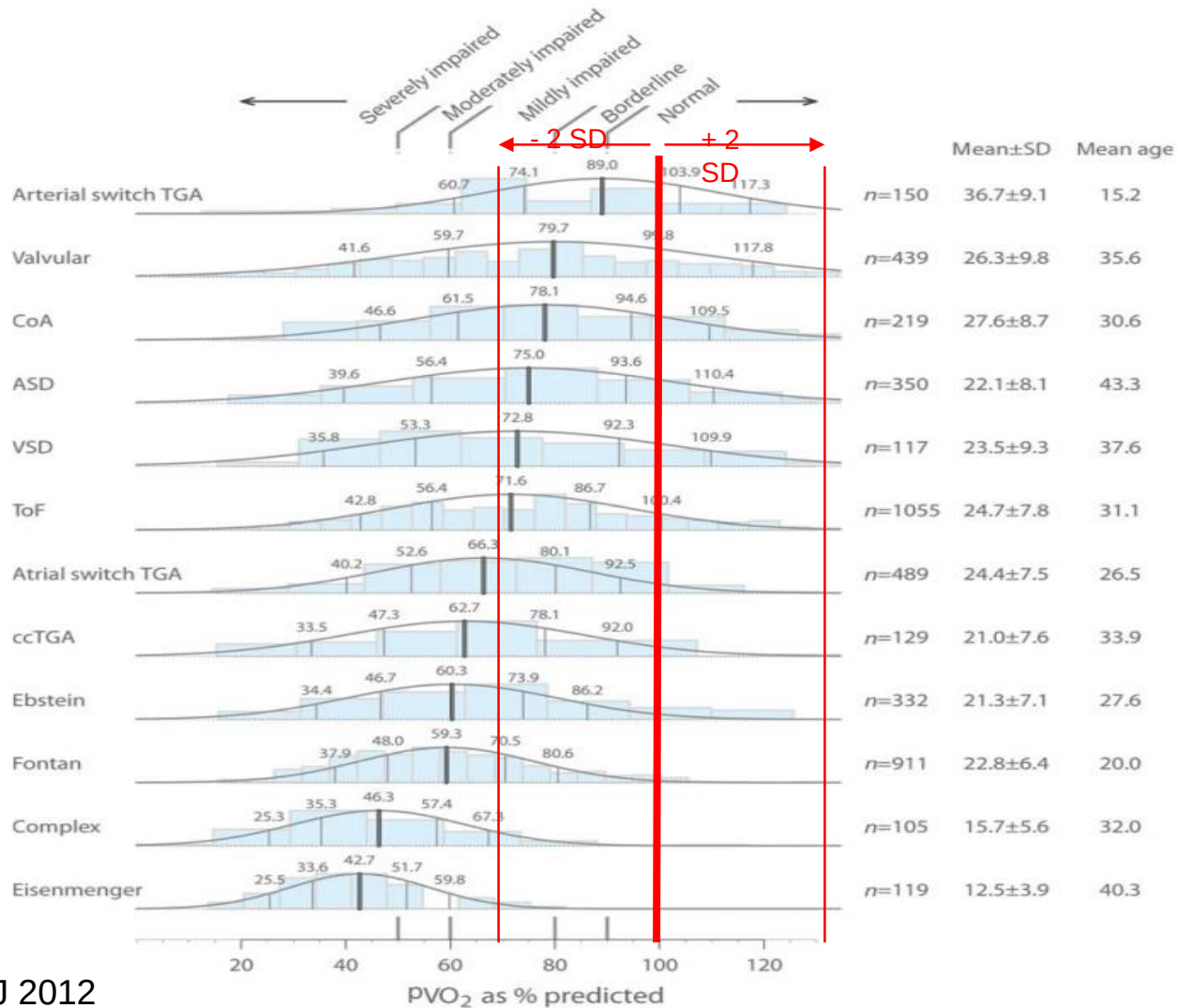


Guidance



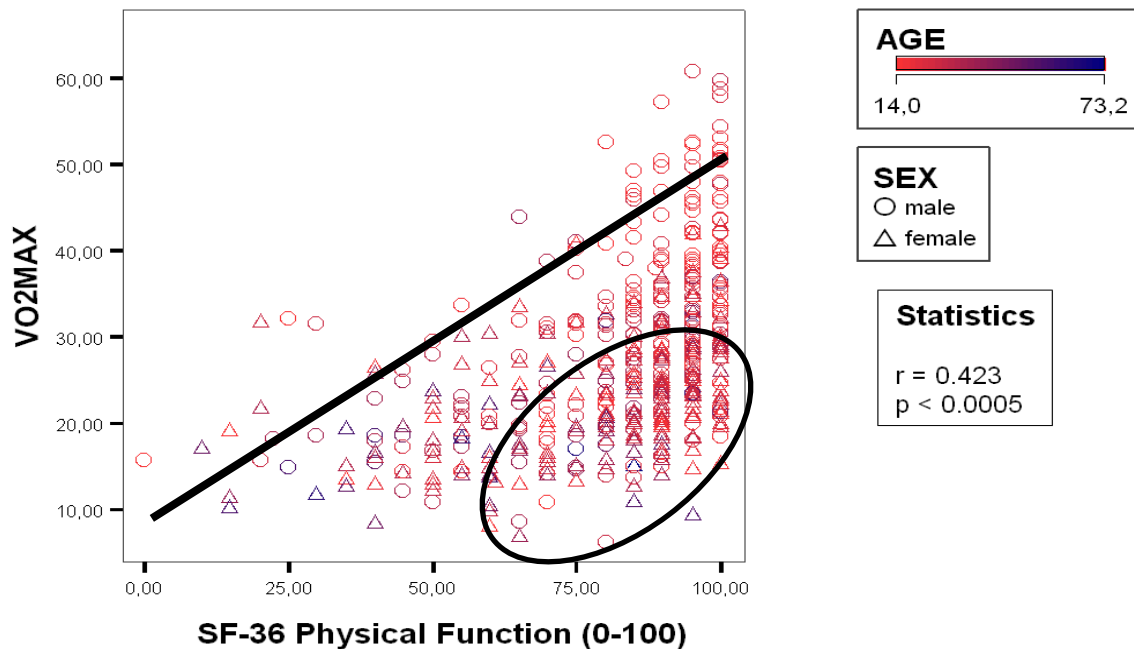
Counseling





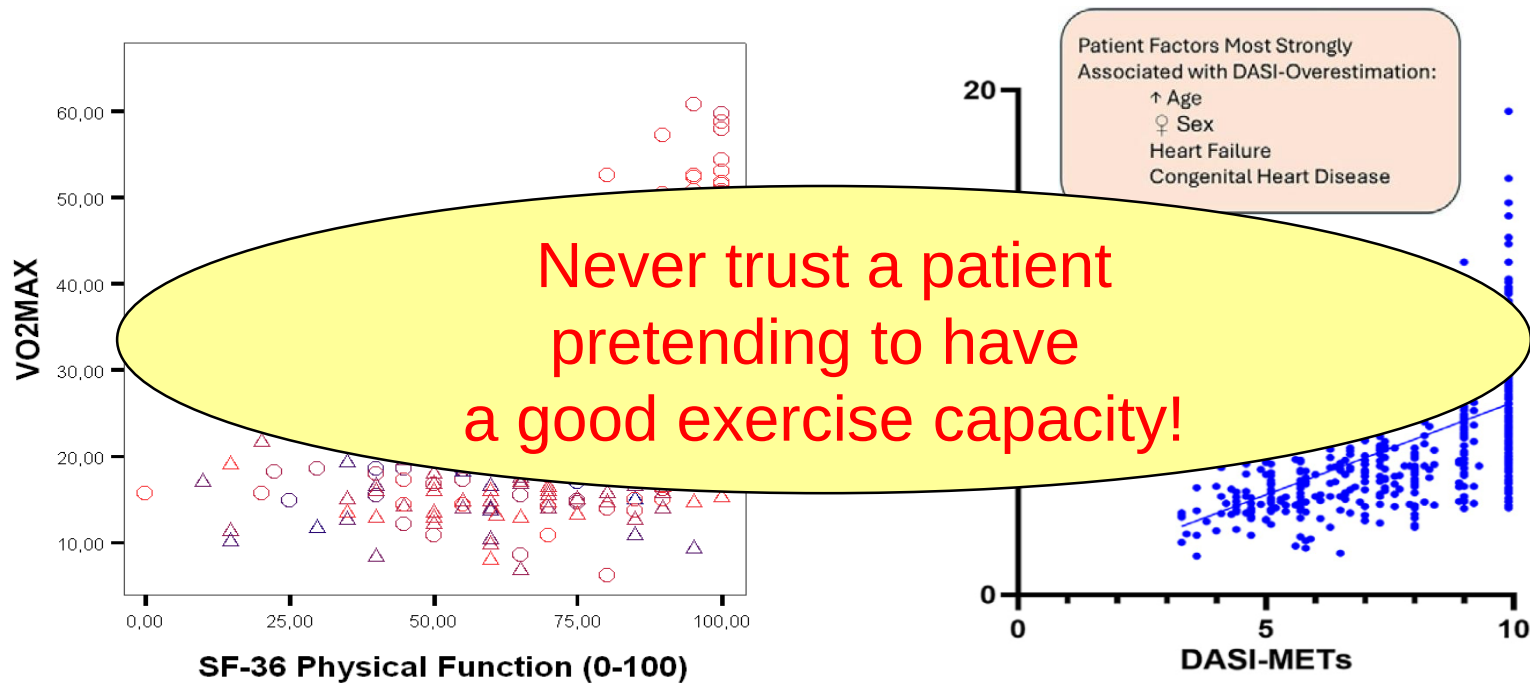


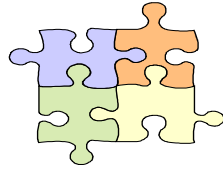
Subjective versus measured exercise capacity





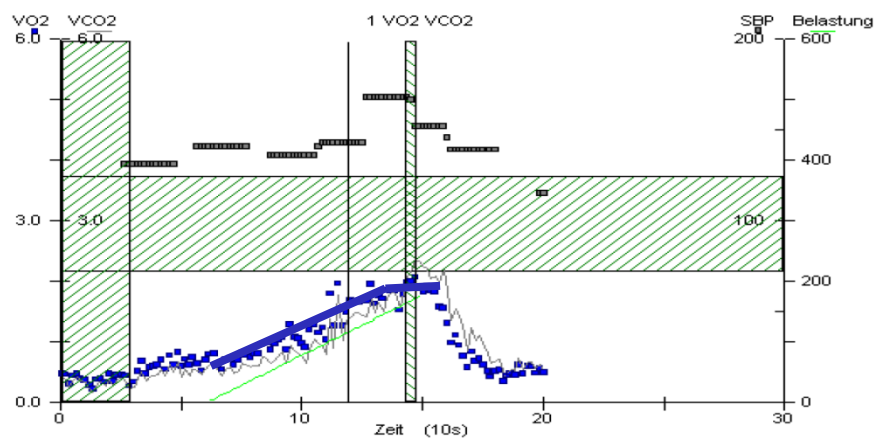
Subjective versus measured exercise capacity



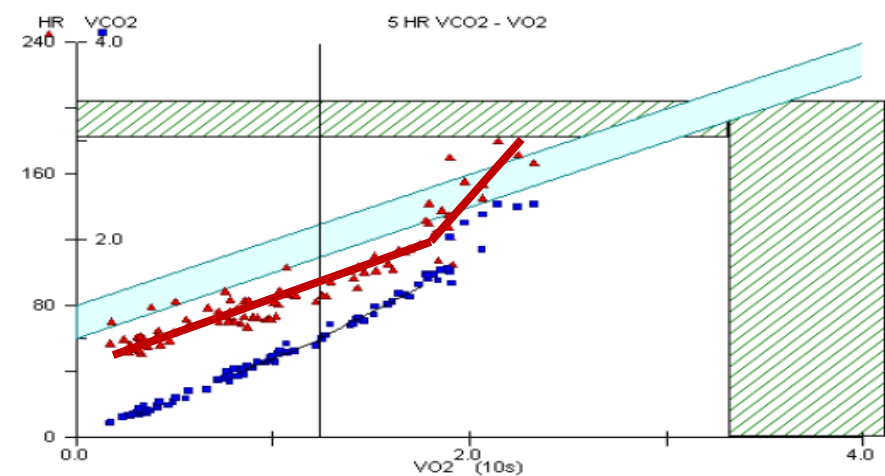


CPET as Diagnostic Tool

- acute circulatory failure at exercise
- RL shunt at exercise
- pulmonary arterial hypertension
- unilateral pulmonary stenosis

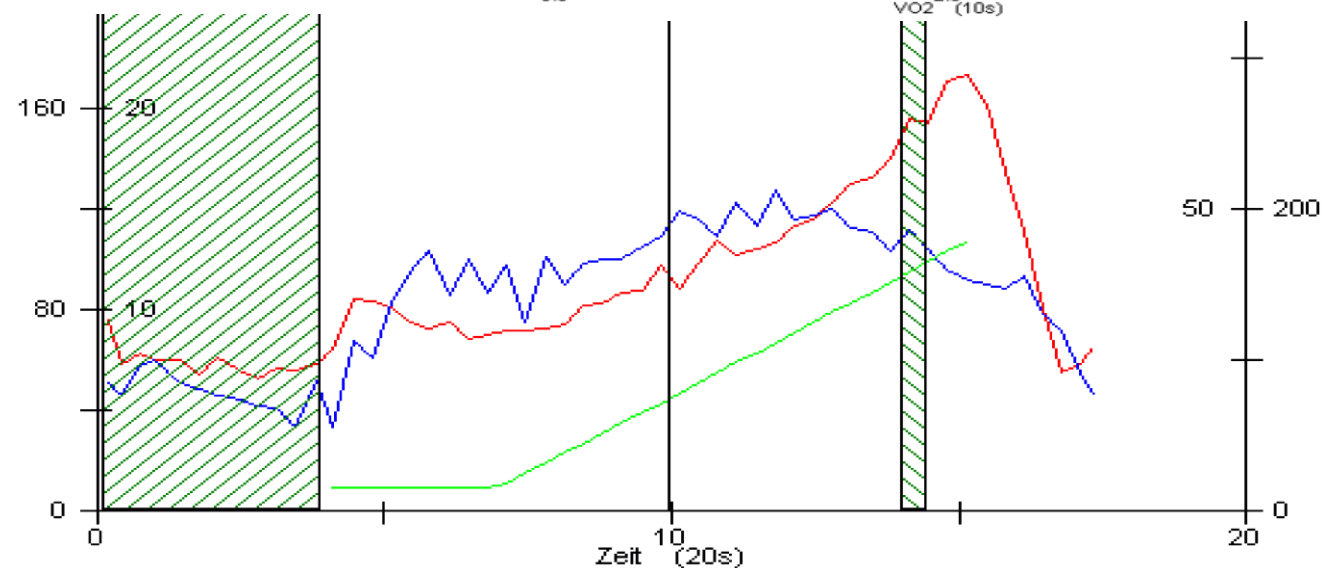


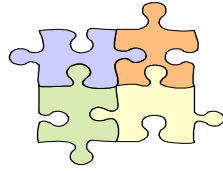
0



male
EBS, WPW
after TV repair
169 cm, 71 kg

RV failure
at high
work load

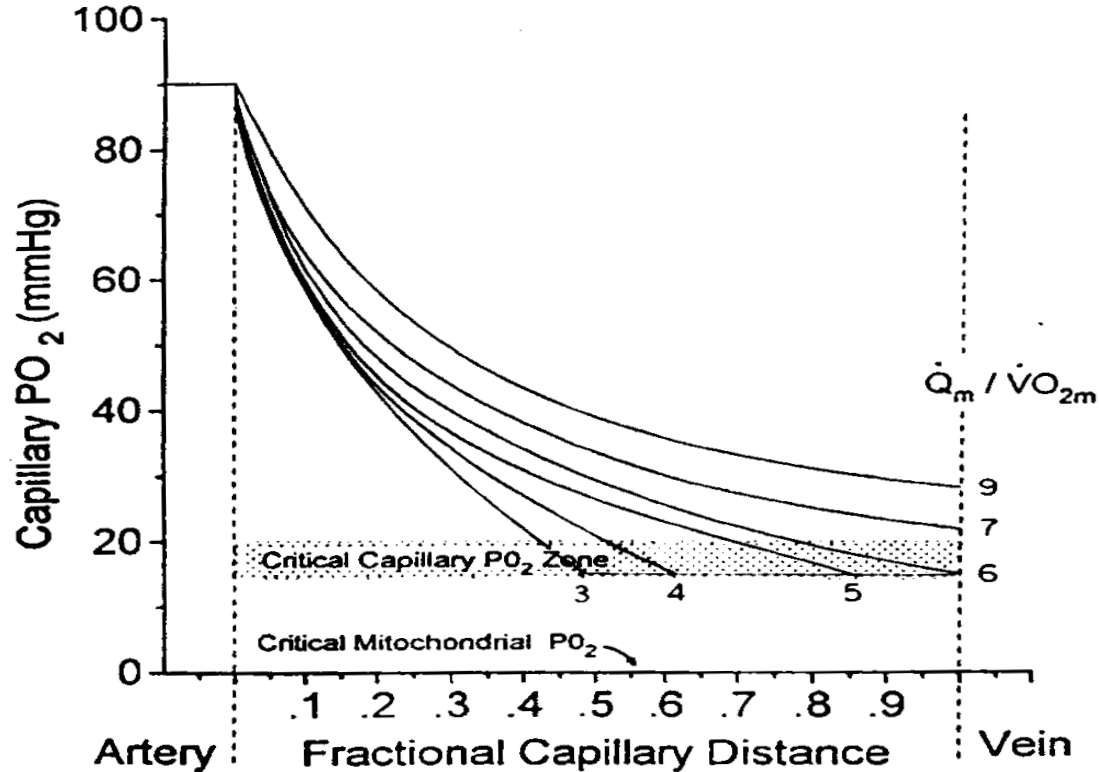
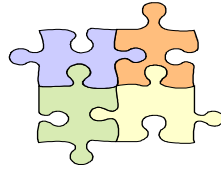


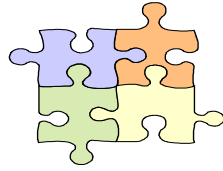


Shunt

- Desoxyhemoglobin shunts into the systemic arteries (right-left shunt)
- Oxyhemoglobin shunts into the pulmonary artery (left-right shunt)

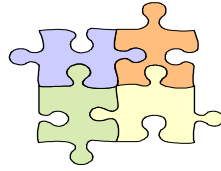
Physiologic Left-Right Shunt





Left-Right Shunt

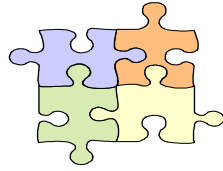
- physiologic (inability for complete extraction)
- functional
 - organs with low O_2 consumption (kidneys, gut)
 - temperature regulation (sweating, fever)
 - perfusion dysregulation
- anatomic
 - av malformation
 - isolated cardiac shunts (ASD, VSD, PDA, ...)



Left-Right Shunt

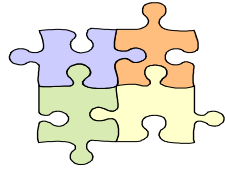
- reduced
 - work load, $\dot{V}O_2/WR$
 - peak $\dot{V}O_2$, VAT, flat O_2 pulse
 - peak circulatory power, peak circulatory flow
- delayed recovery $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E$, HF
- only slightly increased $\dot{V}_E/\dot{V}CO_2$ slope
- Hyperperfusion of the lungs → pulmonary vascular disease
 - exercise induced PAH (exercise echocardiography)
 - potentially shunt reversal (Hypoxämia)

similar to
deconditioning,
early heart failure
or anemia



Shunt

- Oxyhemoglobin shunts into the pulmonary artery (left-right shunt)
- Desoxyhemoglobin shunts into the systemic arteries (right-left shunt)



Hypoxemia

- Reduced inspired PO_2 (hypobaric or hypoxic)
- Hypoventilation
- Regionally reduced ventilation/perfusion ratio
- Diffusion limitations
- Mismatch $C_{pa}O_2$ – perfusion – diffusion
- True Shunt
 - Non ventilated alveoli
 - Intrapulmonary anatomic shunts
 - Veno-venous vessel anomalies
 - cardiac RL shunt



test with
 $F_I O_2 = 100\%$

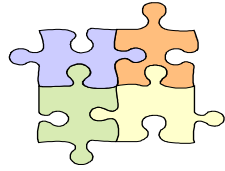
increase in $P_A O_2$

$\Delta S_p O_2 > 10\%$



Hyperoxia test

$\Delta S_p O_2 \leq 10\%$



Hypoxemia

- Reduced inspired PO_2 (hypobaric or hypoxic)
- Hypoventilation
- Regionally reduced ventilation/perfusion ratio
- Diffusion limitations
- Mismatch $C_{pa}O_2$ – perfusion – diffusion
- True Shunt
 - Non ventilated alveoli
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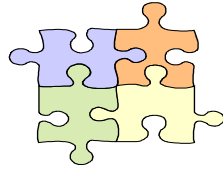


normal
 $P_{A-a}O_2$



elevated
 $P_{A-a}O_2$

$$P_{A-a}O_2 = F_{IO_2} \cdot (P_b - 47\text{mmHg}) - P_ACO_2 / RER \cdot [1 - F_{IO_2} \cdot (1 - RER)] - P_aO_2$$



Hypoxemia

- Reduced inspired PO_2 (hypobaric or hypoxic)
- Hypoventilation
- Regionally reduced ventilation/perfusion ratio
- Diffusion limitations
- Mismatch $C_{pa}O_2$ – perfusion – diffusion
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 - cardiac RL shunt



ONLY
desoxy-HB

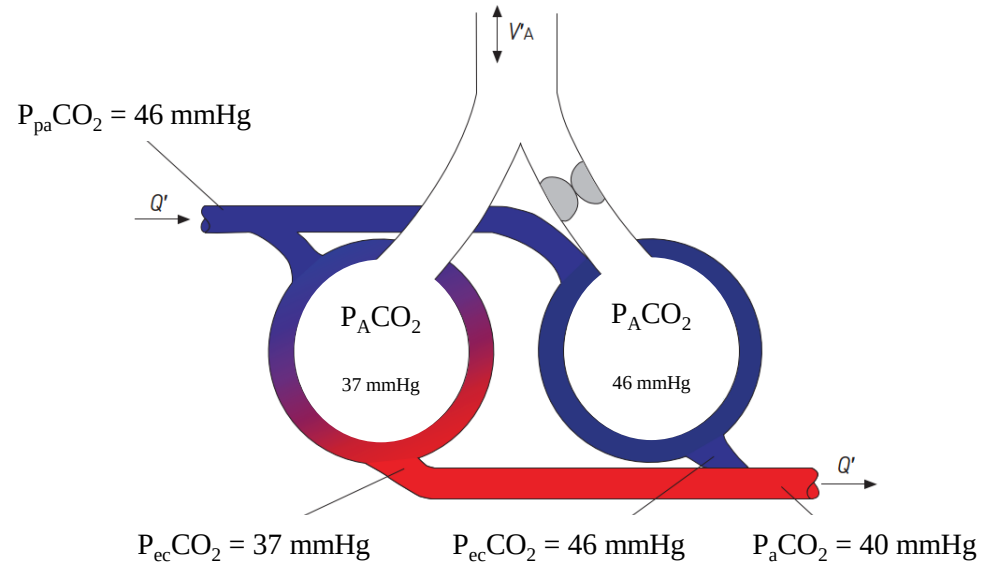


desoxy-HB
+
 CO_2

True Shunt

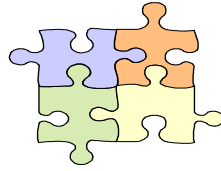
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Alveolar Dead Space



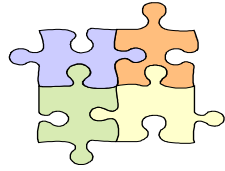
	Compartment 1 (shunt)	Compartment 2 (ventilated)	Combined output
V'_A	0.0 L·min ⁻¹	4.5 L·min ⁻¹	4.5 L·min ⁻¹
Q'	1.5 L·min ⁻¹	3.0 L·min ⁻¹	4.5 L·min ⁻¹
V'_A/Q'	0.0 L·L ⁻¹	1.5 L·L ⁻¹	1.0 L·L ⁻¹
$P_a\text{CO}_2$	46 mmHg	37 mmHg	40 mmHg
$P_A\text{CO}_2$	46 mmHg	37 mmHg	37 mmHg
Alveolar V_D/V_T			7.5%

V'_A : alveolar ventilation; Q' : perfusion; $P_a\text{CO}_2$: arterial CO_2 tension; $P_A\text{CO}_2$: alveolar CO_2 tension; V_D/V_T : alveolar dead space. $= (P_a\text{CO}_2 - P_E\text{CO}_2) / P_a\text{CO}_2$



Right-Left Shunt

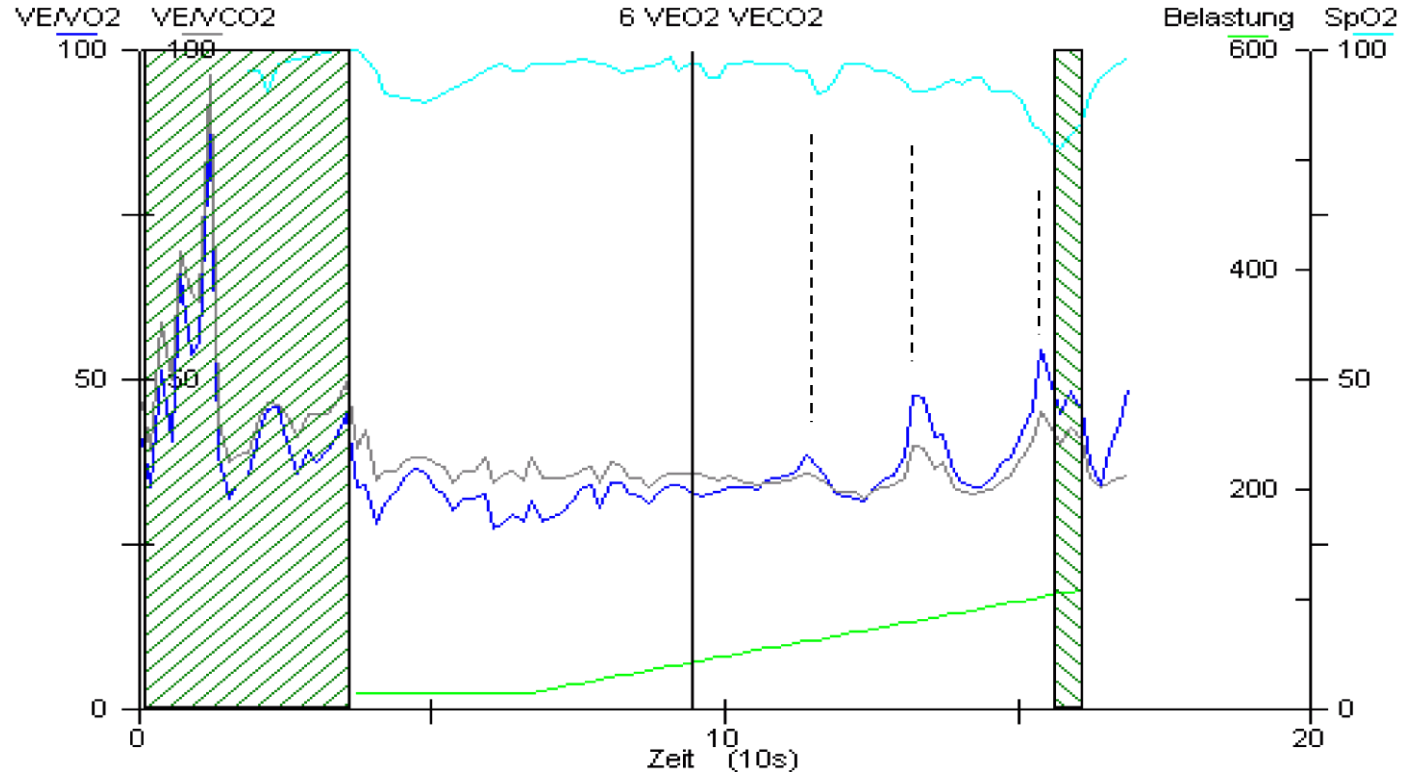
- S_pO_2 decrease
 - O_2 pulse + $\dot{V}O_2$ flattening, $HR/\dot{V}O_2$ kinking
 - decreased peak $\dot{V}O_2$, peakCP, peakCW
- excessive ventilatory drive, increased V_D/V_T
 - $\dot{V}_E$ increases, RER increases
 - ventilatory equivalents increase (O_2 + CO_2 in parallel)
 - $P_{ET}O_2$ increases, $P_{ET}CO_2$ decreases

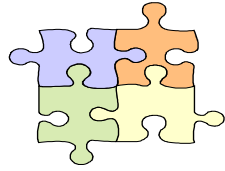


Right-Left Shunt (4)

23 year
old female,
PAH, PFO,
163 cm,
64 kg

RL shunt
with
PAH crises

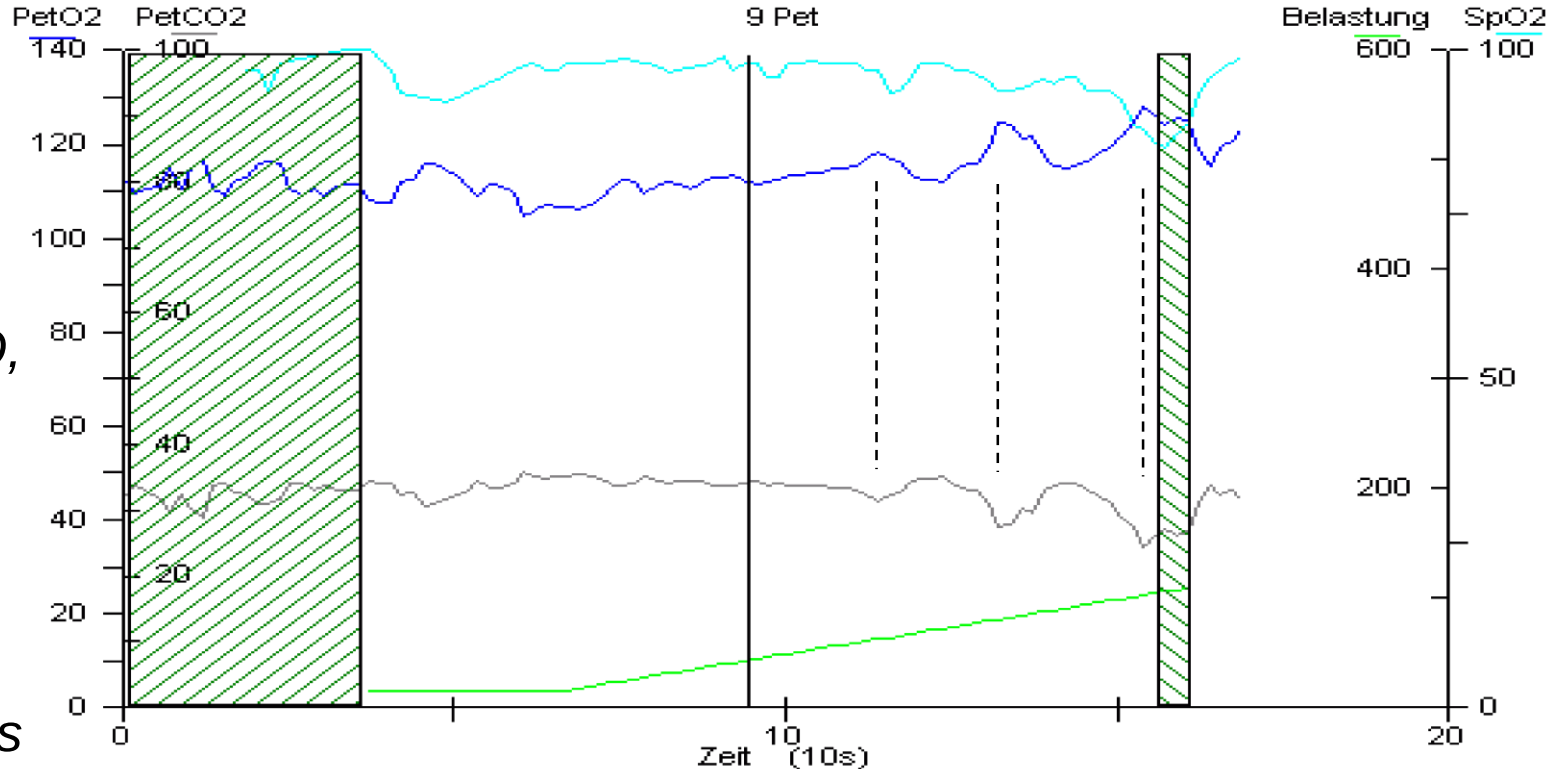


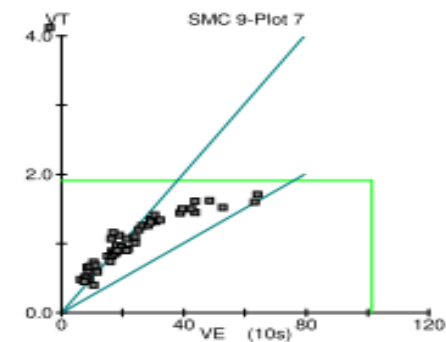
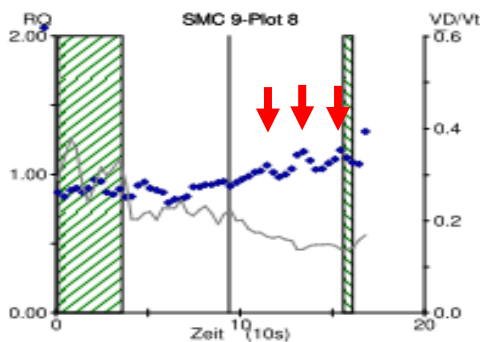
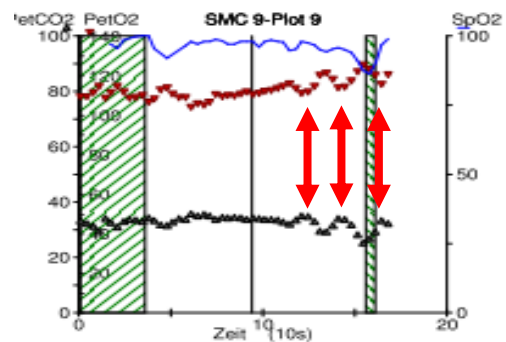
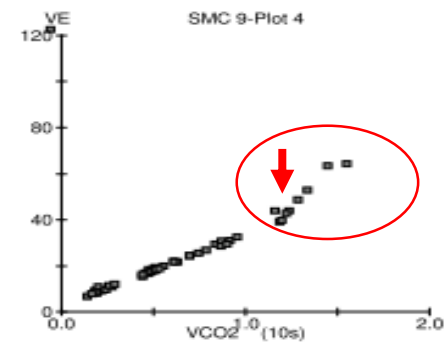
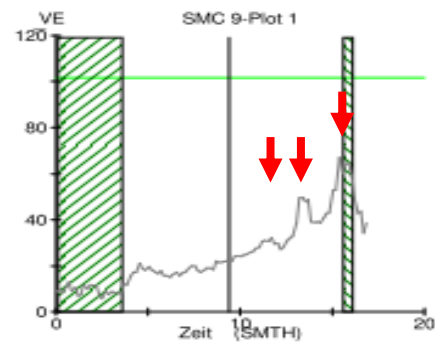
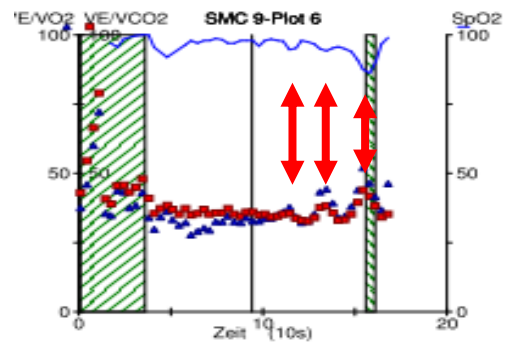
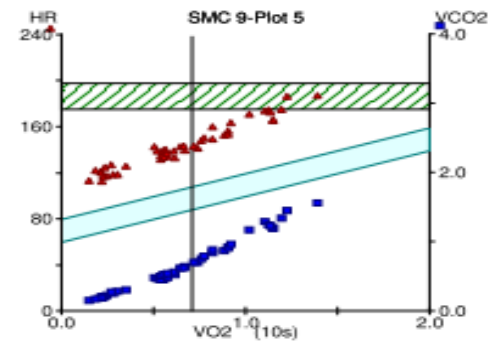
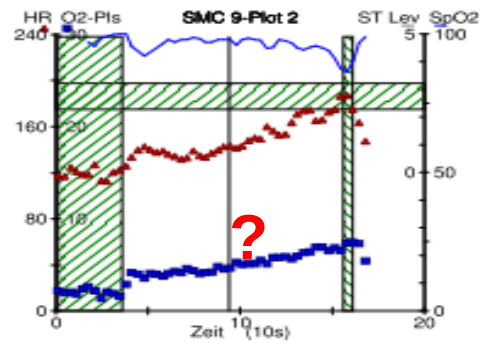
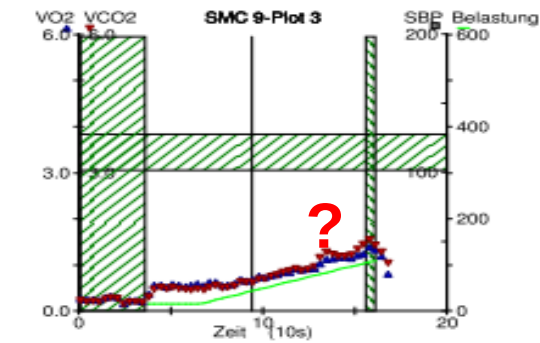


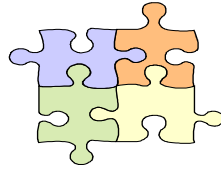
Right-Left Shunt (7)

*female,
23 years,
PAH, PFO,
163 cm,
64 kg*

*RL shunt
with
PAH crises*







$\dot{V}_E / \dot{V}CO_2$ slope increase

- Left/right heart failure with elevated $\dot{V}/\dot{Q}$
- Pulmonary (arterial) hypertension
- RL shunt
- $\dot{V}/\dot{Q}$ mismatch
 - unilateral pulmonary artery stenosis
 - stenosis of small pulmonary arteries
 - aortopulmonary collaterals
 - pulmonary vein stenosis
- Increased ventilatory drive (ergoreceptor reflex, chemoreceptor sensibility, ...)

iCPET (with Swan-Ganz-Cath.)

Exercise PH:

PAP/CO-slope > 3 mmHg/L/min (< 60 yr)

postcapillary exercise PH:

PAWP/CO-slope > 2 mmHg/L/min

iCPET in Fontan

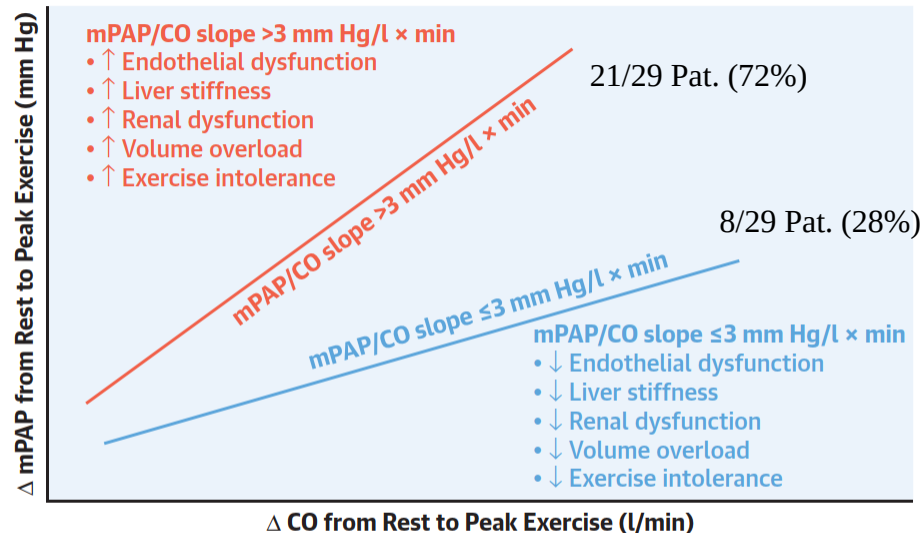
TABLE 2 Rest Hemodynamics

	All (N = 29)	mPAP/CO Slope >3		p Value
		No (n = 8)	Yes (n = 21)	
Mixed venous saturation, %	63 ± 7	65 ± 6	62 ± 5	0.20
Pulmonary venous saturation, %	94 ± 2	95 ± 2	94 ± 3	0.60
Systemic saturation, %	94 ± 3	94 ± 2	93 ± 2	0.60
Heart rate, beats/min	72 ± 9	71 ± 7	77 ± 8	0.07
CVP, mm Hg	15 ± 4	12 ± 2	16 ± 3	0.002
PAWP, mm Hg	11 ± 4	8 ± 2	12 ± 4	0.01
TPG, mm Hg	4 ± 2	4 ± 1	4 ± 2	0.60
Systolic blood pressure, mm Hg	116 ± 14	110 ± 9	119 ± 13	0.30
Diastolic blood pressure, mm Hg	66 ± 14	64 ± 10	67 ± 14	0.60
Mean blood pressure, mm Hg	84 ± 13	83 ± 11	84 ± 13	0.40
Qp index, l/min/m ²	2.3 ± 0.9	2.5 ± 0.6	2.2 ± 0.7	0.30
PVR index, WU · m ²	1.7 ± 0.6	1.6 ± 0.5	1.8 ± 0.6	0.40
Qs index, l/min/m ²	2.3 ± 0.8	2.5 ± 0.4	2.2 ± 0.5	0.20
Qp/Qs	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	0.80
SVI, ml/m ²	32 ± 8	35 ± 5	29 ± 7	0.04
SVR index, WU · m ²	30 ± 11	28 ± 10	31 ± 8	0.50

Values are mean ± SD.

CVP = central venous pressure; mPAP/CO slope = slope of mean pulmonary artery pressure versus cardiac output; PAWP = pulmonary artery wedge pressure; PVR = pulmonary vascular resistance; Qp = pulmonary blood flow; Qs = systemic blood flow; SVI = stroke volume index; SVR = systemic vascular resistance; TPG = transpulmonary gradient; WU = Wood unit.

CENTRAL ILLUSTRATION Schematic Showing the Relationship Between Pulmonary VR and End-Organ Function



Egbe, A.C. et al. J Am Coll Cardiol. 2020;76(23):2755-63.

Pressure-flow relationship showing change in mean pulmonary artery pressure (mPAP) (Fontan pressure) per unit change in cardiac output (CO), or mPAP/CO slope, during exercise. Abnormal pulmonary vascular reserve (VR) defined as mPAP/CO slope >3 (red) is associated with worse endothelial dysfunction and end-organ dysfunction (more liver stiffness, renal dysfunction, volume overload, and exercise intolerance) as compared to normal pulmonary VR defined as mPAP/CO slope ≤3 (blue).

iCPET in Fontan

Definitions

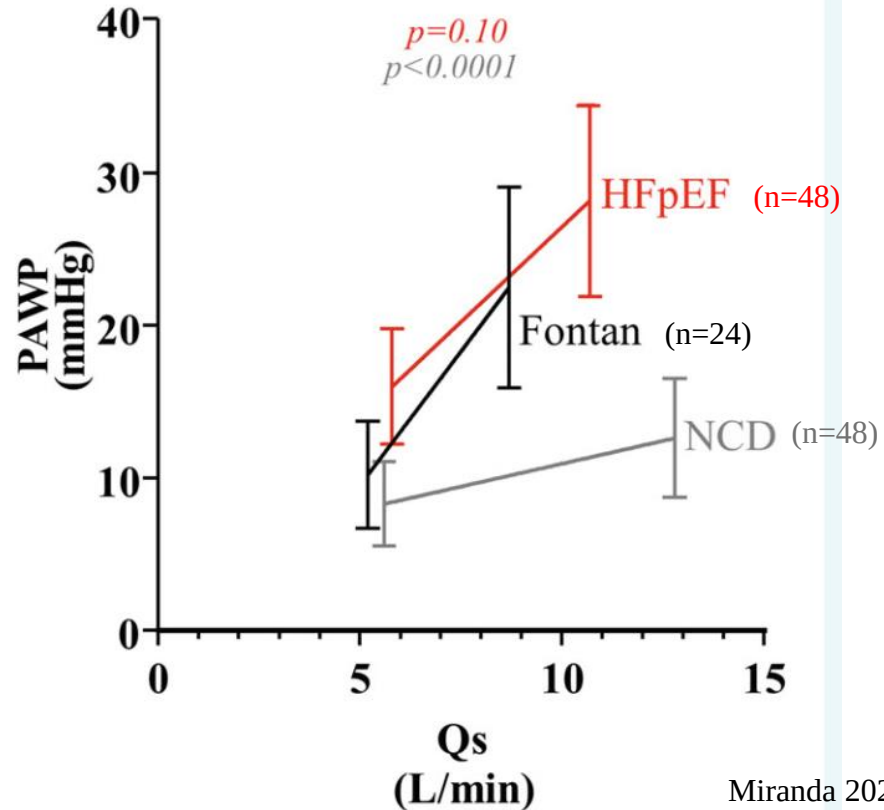
Exercise PH

$$\Delta\text{PAP}/\Delta\text{Qp} > 3 \text{ mmHg/L/min}$$

postcapillary exercise PH

$$\Delta\text{PAWP}/\Delta\text{Qs} > 2 \text{ mmHg/L/min}$$

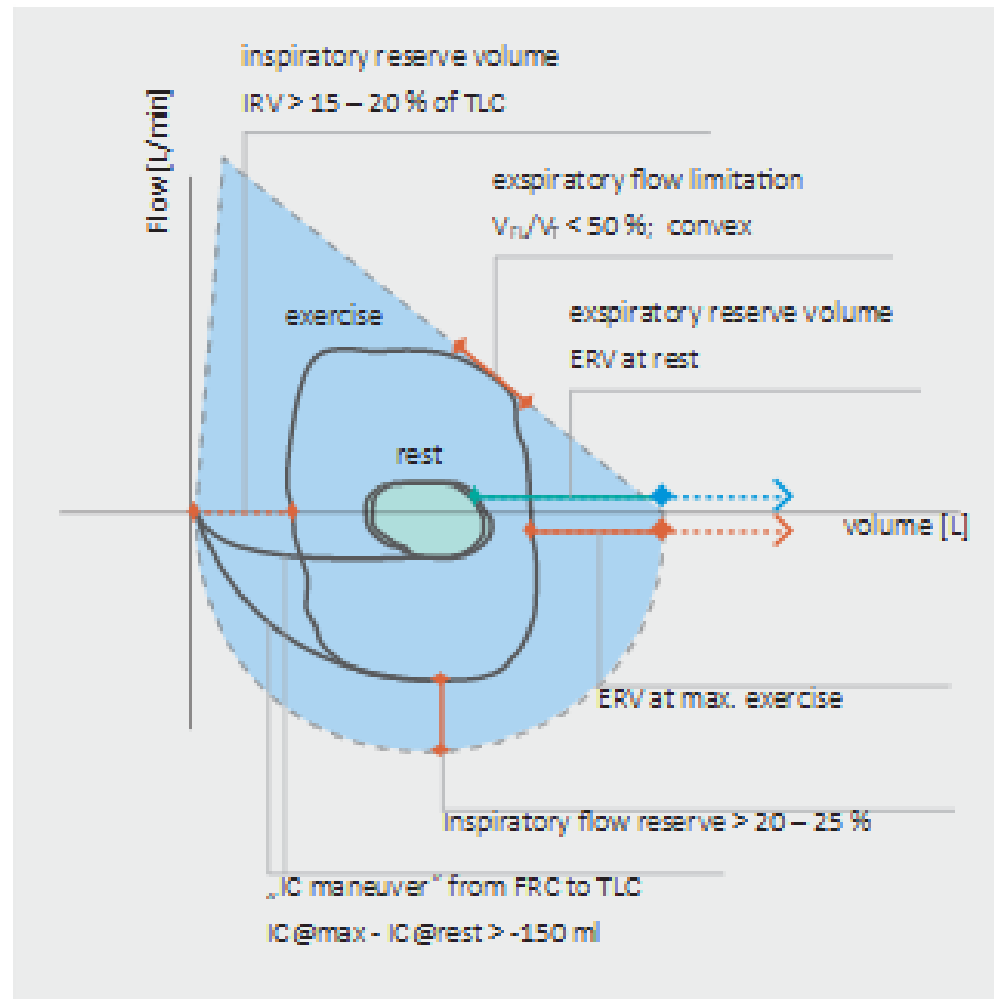
2022 ESC/ERS Guidelines PH (mod)



IC Maneuver

Obstructive Dynamic Hyperinflation

- IC decrease > 150 mL
- $V_{FL}/V_T > 50\%$
- concave/straight expir. shape of the F/V curve



IC Maneuver in CHD

Obstructive Dynamic Hyperinflation

	Healthy	CHD	CHD
• IC decrease	35.8 %	22.7 %	BR↑, $\dot{V}'O_2\downarrow$, $\dot{V}'E/\dot{V}'CO_2$ -slope↑
• V_{FL}/V_T	34.3 %	33.5 %	BR↓, $\dot{V}'O_2\downarrow$, $\dot{V}'E/\dot{V}'CO_2$ -slope↑
• Concavity	1.5 %	5.2 %	BR↓, $\dot{V}'O_2\downarrow$, $\dot{V}'E/\dot{V}'CO_2$ -slope↑
• All of them	0.0 %	0.7 %	BR↓, $\dot{V}'O_2\downarrow$, $\dot{V}'E/\dot{V}'CO_2$ -slope↑

IC Maneuver in CHD

Obstructive Dynamic Hyperinflation

- | | Healthy | CHD | CHD |
|----------------|---------|-----|---|
| • IC decrease | | | $\Delta P \uparrow$, $V'O_2 \downarrow$, $V'E/V'CO_2$ -slope $\uparrow$ |
| • V_{FL}/V_T | | | $V'O_2 \downarrow$, $V'E/V'CO_2$ -slope $\uparrow$ |
| • Conc | | | $V'E/V'CO_2$ -slope $\uparrow$ |
| • All of the | | | $V'O_2 \downarrow$, $V'E/V'CO_2$ -slope $\uparrow$ |
- Obstructive Dynamic Hyperinflation is very rare in patients with CHD.
- IC maneuvers are only warranted in patients with suspected COPD.

CPET for Risk Assessment



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EXERCISE CAPACITY AND MORTALITY AMONG MEN REFERRED FOR EXERCISE TESTING

JONATHAN MYERS, PH.D., MANISH PRAKASH, M.D., VICTOR FROELICHER, M.D., DAT DO, M.D., SARA PARTINGTON, B.Sc.,
AND J. EDWIN ATWOOD, M.D.

„Survival of the fittest“

1 MET more → 12% longer survival



Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

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Exercise Intolerance in Adult Congenital Heart Disease: Comparative Severity, Correlates, and Prognostic Implication

Gerhard-Paul Diller, Konstantinos Dimopoulos, Darlington Okonko, Wei Li, Sonya V. Babu-Narayan, Craig S. Broberg, Bengt Johansson, Beatriz Bouzas, Michael J. Mullen, Philip A. Poole-Wilson, Darrel P. Francis and Michael A. Gatzoulis

Circulation 2005;112:828-835; originally published online Aug 1, 2005;

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**ACHD with a peakVO₂ < 15.5 ml/kg/min
5.6-fold mortality**

CPET for Risk Assessment



- Fallot tetralogy (*survival*) (Giardini 2007, Müller 2015)
- TGA after Senning/Mustard (*survival without emergency admission*) (Giardini 2009)
- Ebstein (*survival without emergency admission or surgery*) (Radojevic 2011)
- Fontan (*admission*) (Diller 2012)
- Coarctation (*hypertension*) (Buys 2013)
- Cyanotic heart defects (*survival*) (Radke submitted)



CPET to Guide Therapy

- Fallot tetralogy (*survival*) (Giardini 2007, Müller 2015)
- TGA after Senning/Mustard (*survival without emergency admission*) (Giardini 2009)
- Ebstein (*survival without emergency admission or surgery*) (Radojevic 2011)
- Fontan (*admission*) (Diller 2012)
- Coarctation (*hypertension*) (Buys 2013)
- Cyanotic heart defects (*survival*) (Radke submitted)

-> ICD implantation ?

-> Listing for transplant ?

-> regular and frequent ambulatory follow-ups !!!



CPET to Guide Therapy

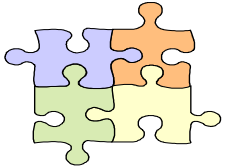
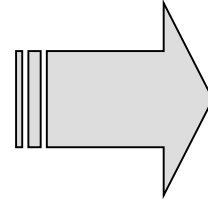
- Fallot tetralogy with
 - severe pulmonary regurgitation
 - only mild RV dilatation
- asymptomatic severe aortic stenosis
- heart failure (CRT implantation, listing for transplant)
- pulmonary arterial hypertension (therapy escalation?)
- Ebstein anomaly (tricuspid repair) ?



Counseling

- Physical activity, sport
- Insurance
- Education, profession, career planning
- Disability assessment
- Retirement

Take-Home Message



CPET is essential
in the management of patients
with congenital heart disease
to evaluate exercise capacity,
to detect diagnostic details,
to make a risk assessment,
to guide therapy,
and to give appropriate advices.



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Head of Exercise Laboratory

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