



Cardiopulmonary Exercise Testing in Heart Failure and Ischemia

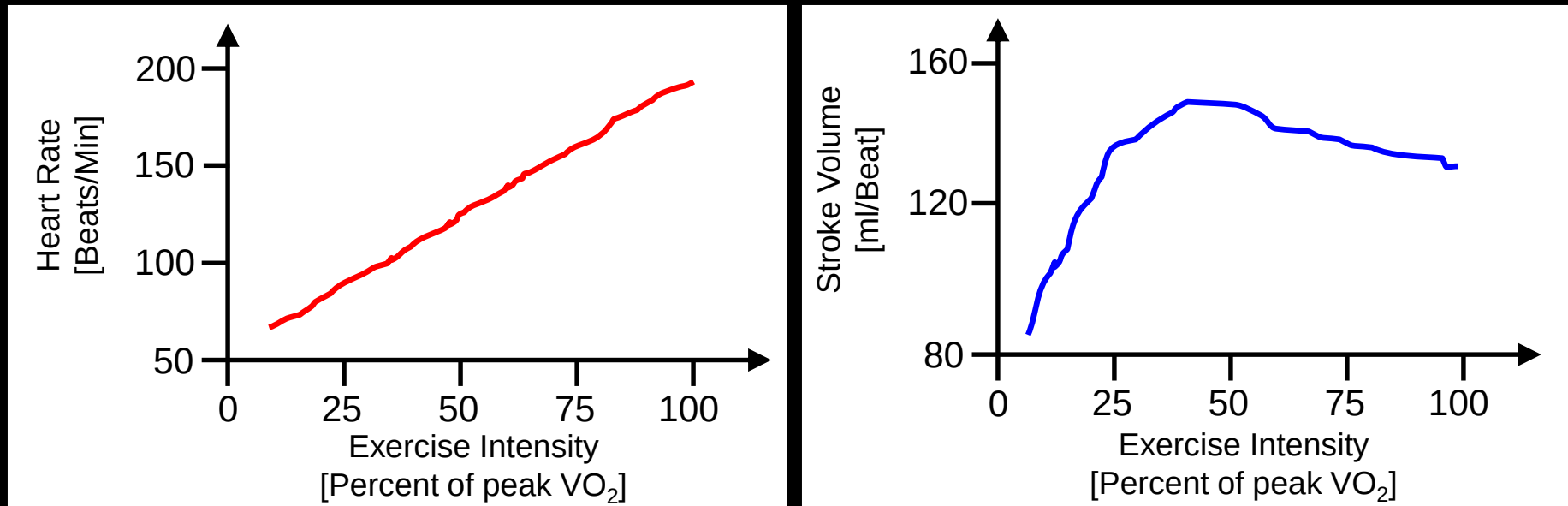
Daniel Dumitrescu

Herz- und Diabeteszentrum NRW

Bad Oeynhausen

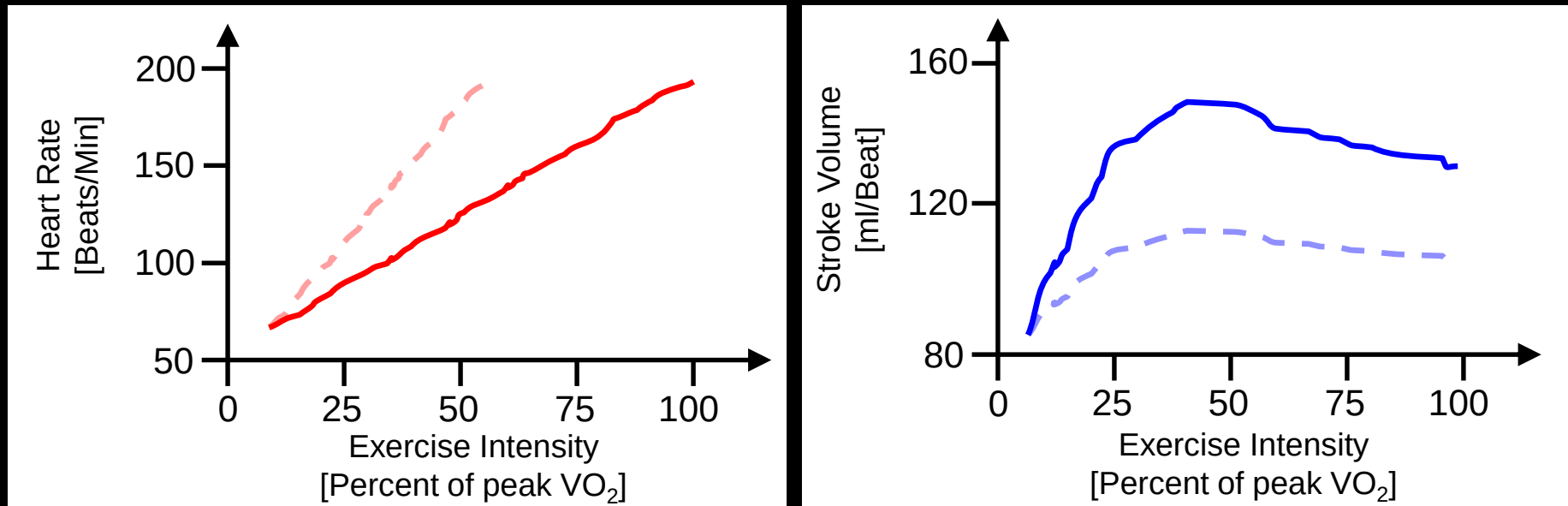
ddumitrescu@hdz-nrw.de

Pathophysiological Considerations



Adapted from: Stringer WW et al . Eur J Appl Physiol 2005; 93: 634-639

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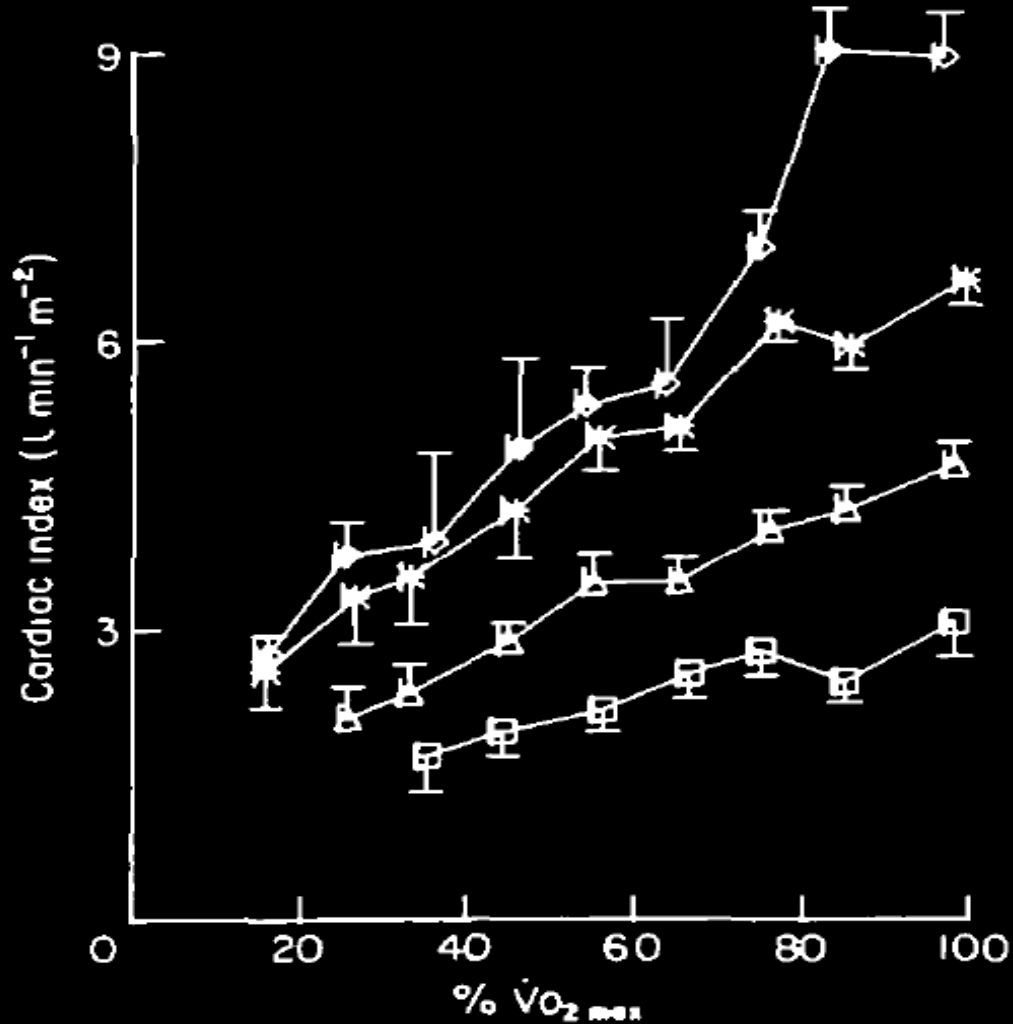
Pathophysiological Considerations

$$VO_2 = \text{Cardiac Output} \times (CaO_2 - CvO_2)$$

Pathophysiological Considerations

$$VO_2 = SV \times HR \times (CaO_2 - CvO_2)$$

Oxygen uptake and hemodynamics



Peak oxygen uptake:

Class A: > 20 ml/min/kg

Class B: 16- 20 ml/min/kg

Class C: 10- 16 ml/min/kg

Class D: < 10 ml/min/kg

Fick Equation for Cardiac Output Determination:

$$\text{CO (HR X SV)} = \frac{\text{VO}_2}{\text{CaO}_2 - \text{CvO}_2}$$

Oxygen uptake and influencing factors

$$VO_2 = HF \times SV \times (CaO_2 - CvO_2)$$

Oxygen uptake and influencing factors

Chronotropic competence
Autonomic nervous system

Ventricular filling
Systolic Funktion
Diastolic Function

$$VO_2 = HF \times SV \times (CaO_2 - CvO_2)$$

Skeletal muscle:
Oxygen extraction
Hemodynamics
Mitochondrial function

O₂ transport capacity:
Hemoglobin content

Oxygen pulse concept

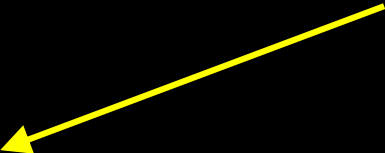
Oxygen pulse = oxygen uptake ÷ heart rate

(Henderson and Prince 1914)

**Oxygen pulse describes
oxygen uptake per heartbeat.**

Fick equation:

$$CO = \frac{VO_2}{CaO_2 - CvO_2}$$

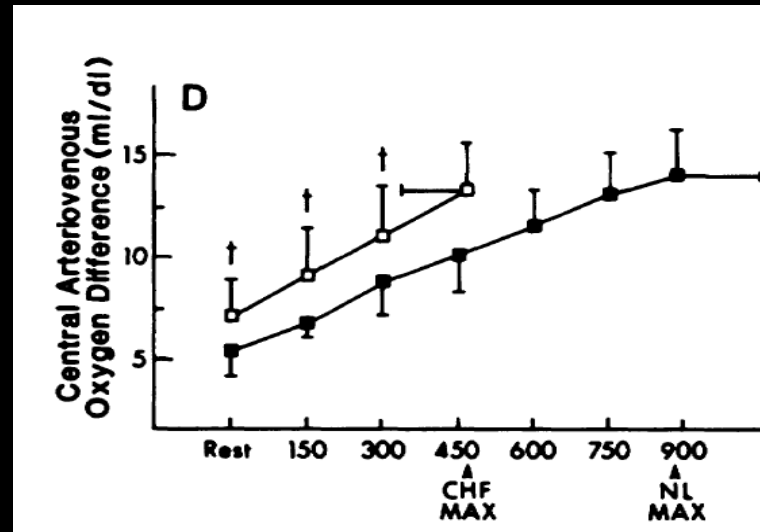
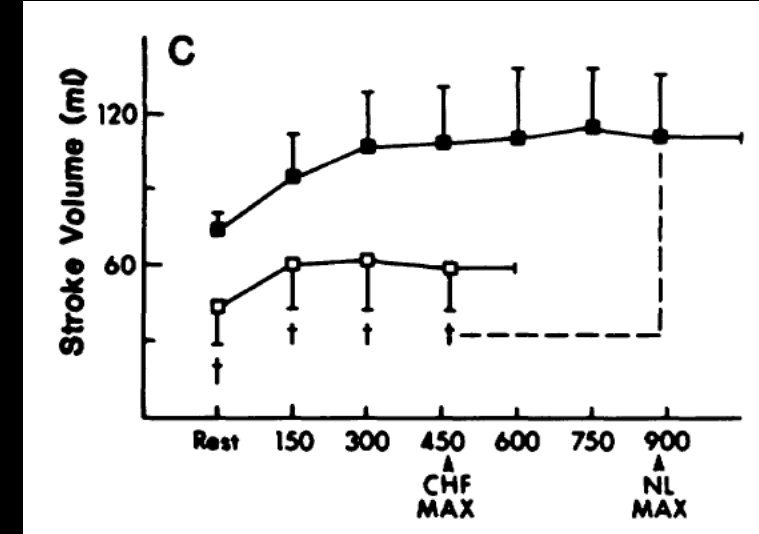
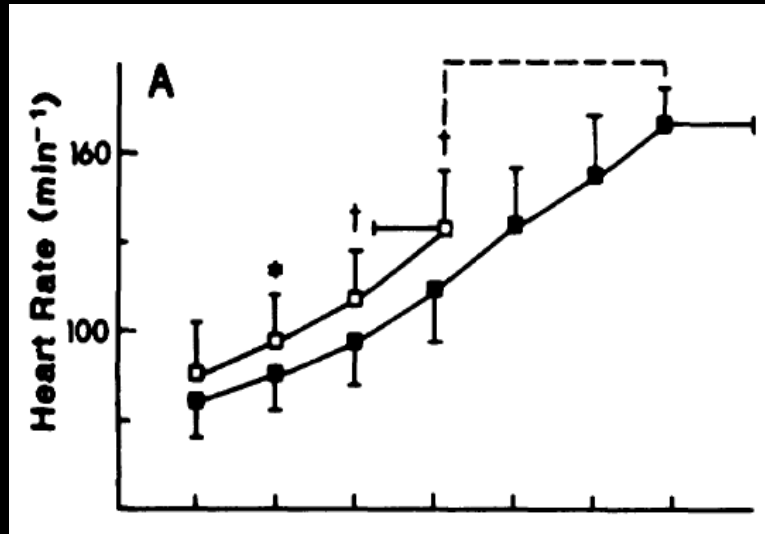

$$SV \times HR = \frac{VO_2}{CaO_2 - CvO_2} \longrightarrow \frac{VO_2}{HR} = SV \times (CaO_2 - CvO_2)$$

**Relation Between Central and Peripheral
Hemodynamics During Exercise in Patients
With Chronic Heart Failure**

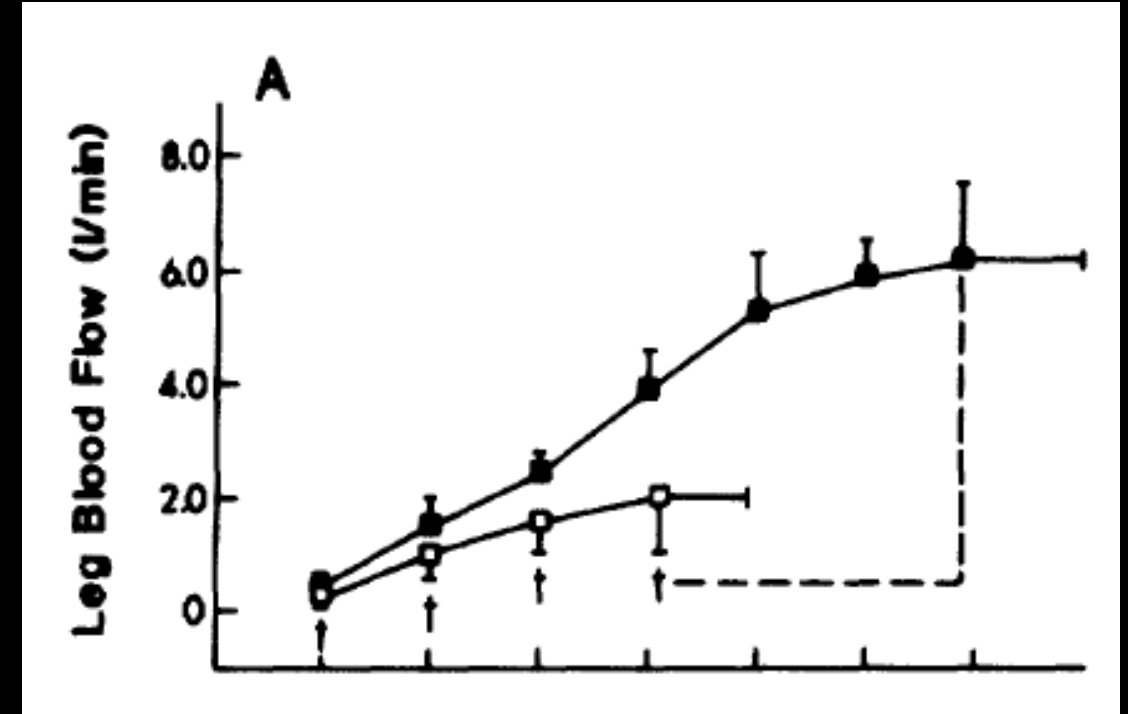
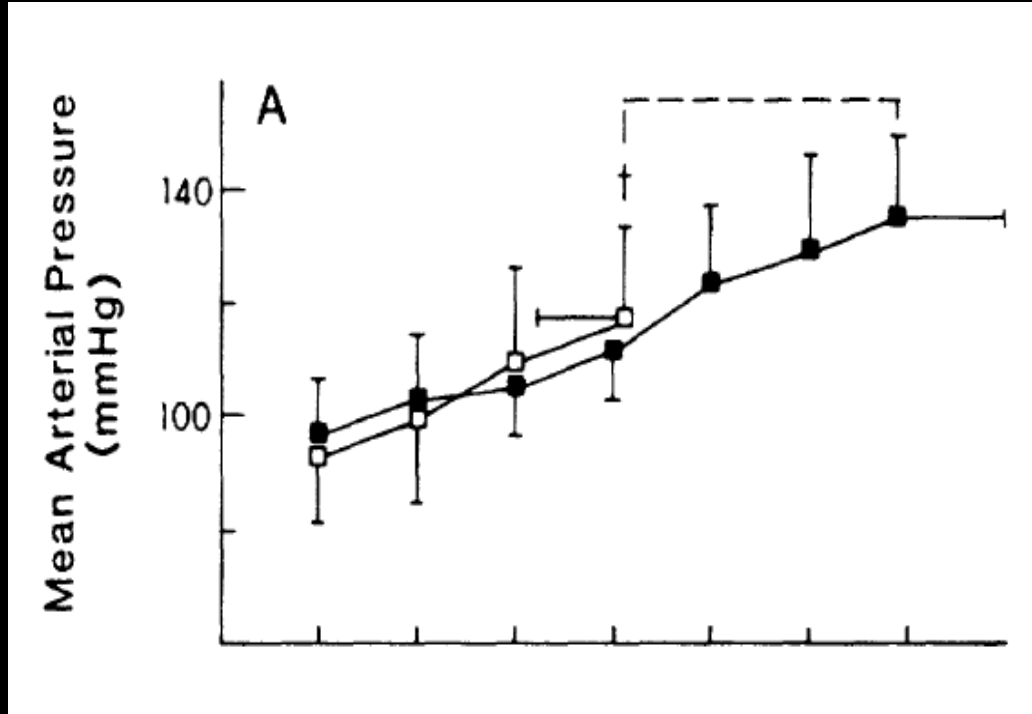
**Muscle Blood Flow Is Reduced With Maintenance of
Arterial Perfusion Pressure**

Martin J. Sullivan, MD, J. David Knight, PhD,
Michael B. Higginbotham, MB, and Frederick R. Cobb, MD

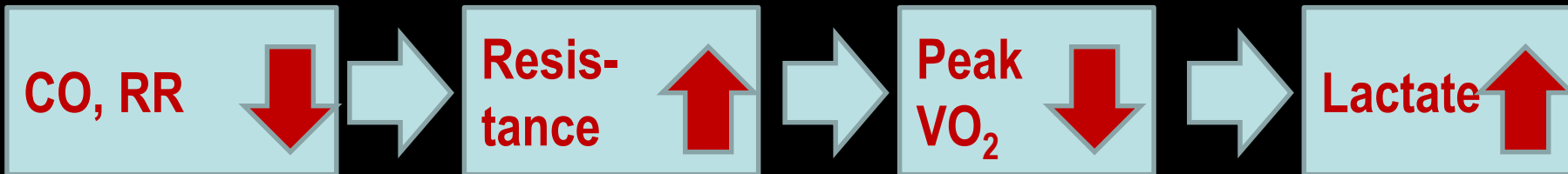
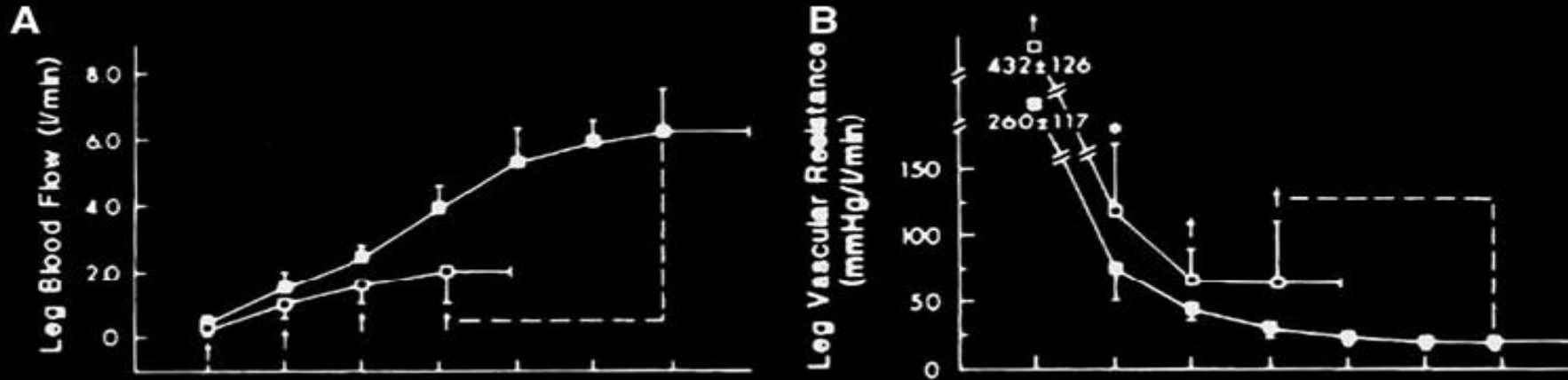
Central and peripheral hemodynamics in heart failure



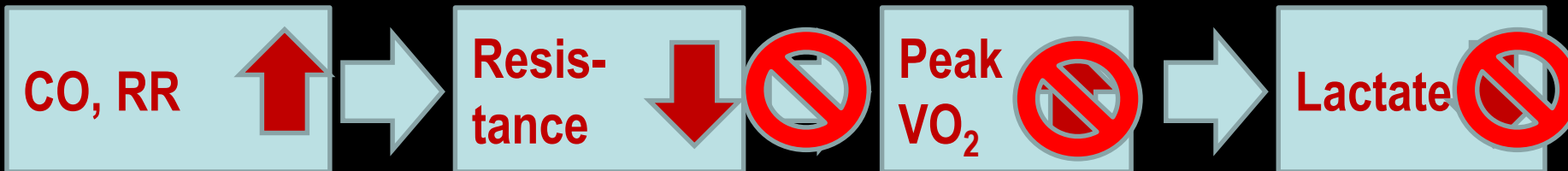
Central and peripheral hemodynamics in heart failure



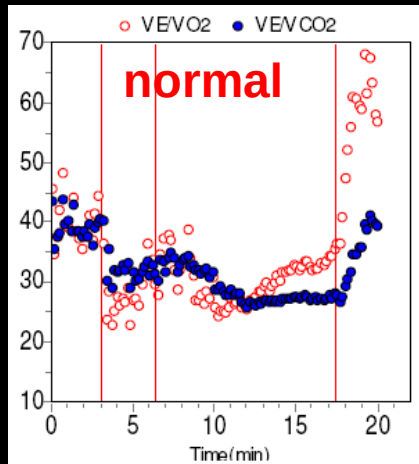
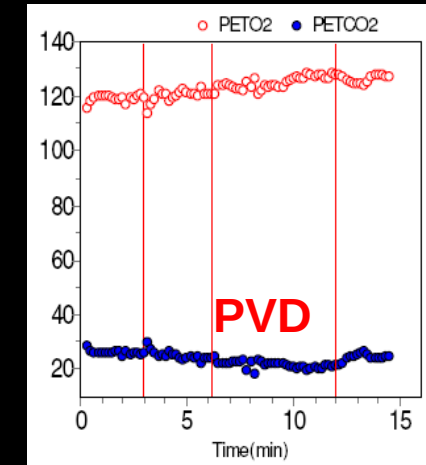
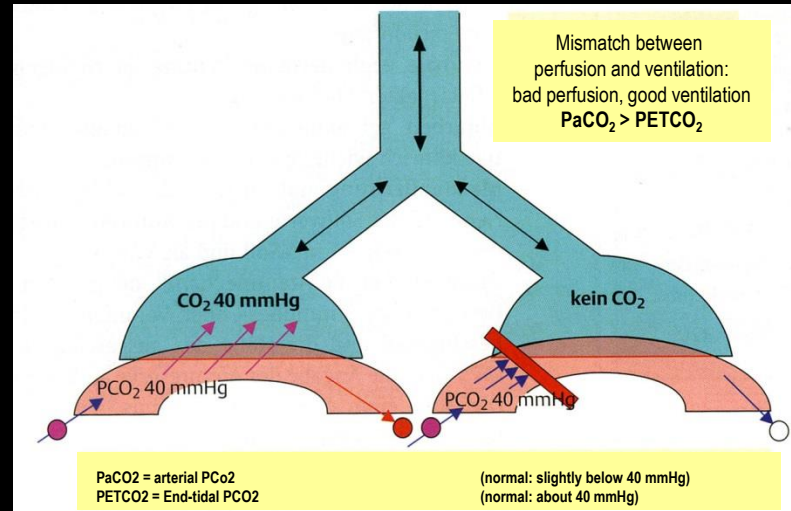
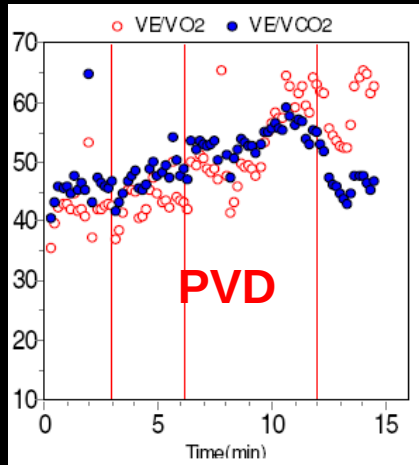
Peripheral distribution of Blood Flow



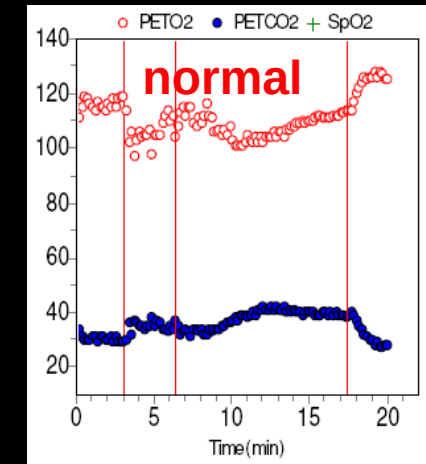
After initiation of therapy:



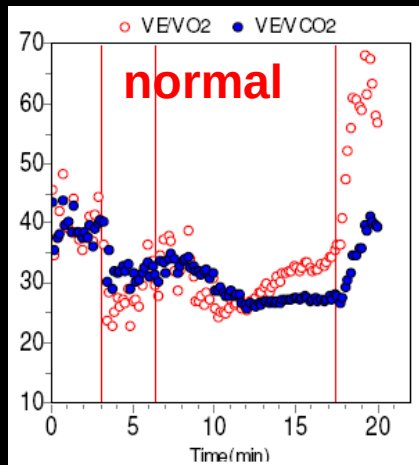
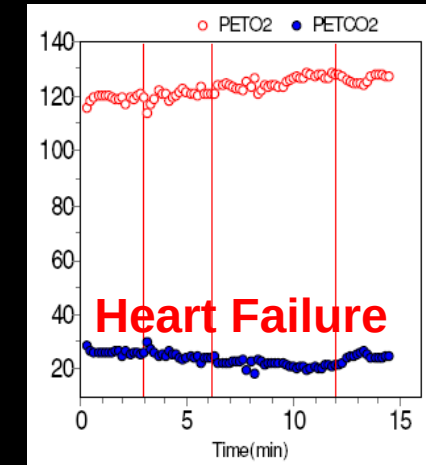
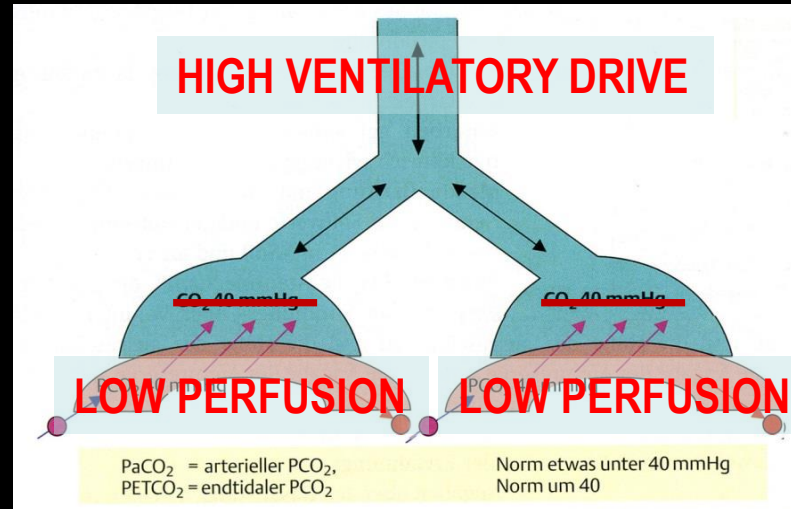
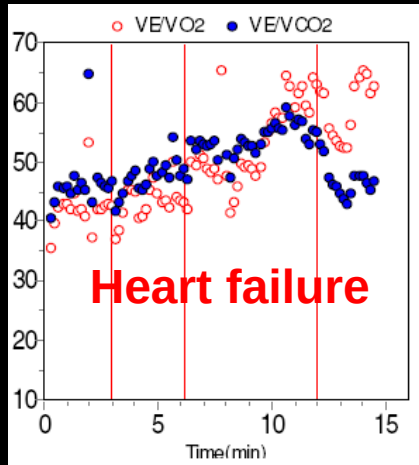
Ventilatory equivalents in the diagnosis of pulmonary vascular disease (PVD)



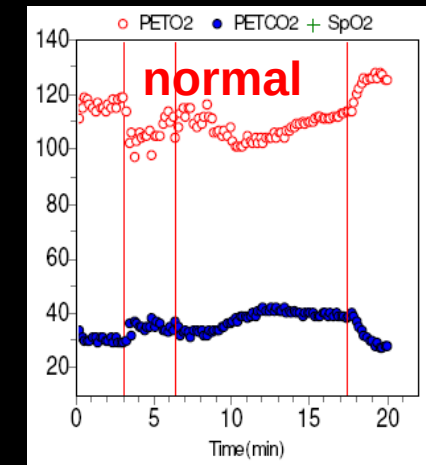
Pulmonary Ventilation-/Perfusion mismatch, reflected by ventilatory efficiency: VE/VCO₂(left) and PETCO₂ (right)



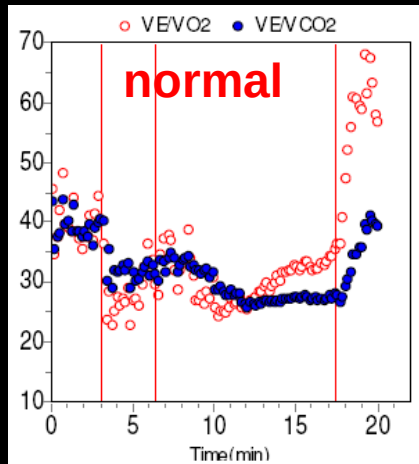
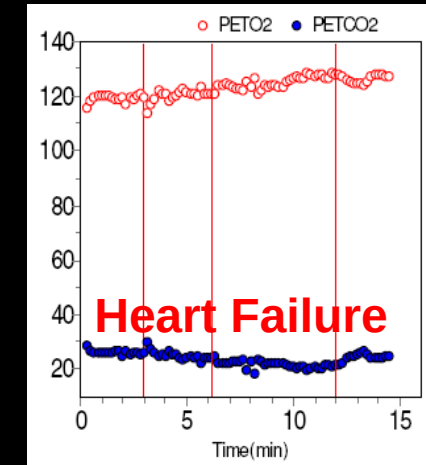
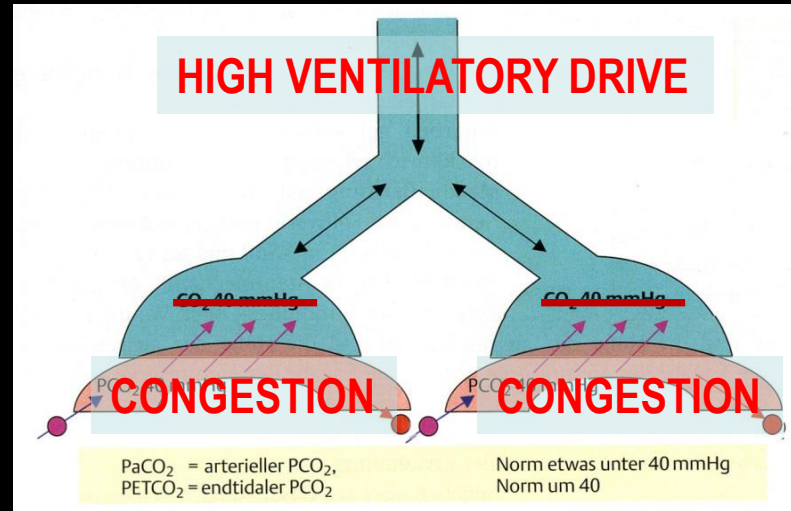
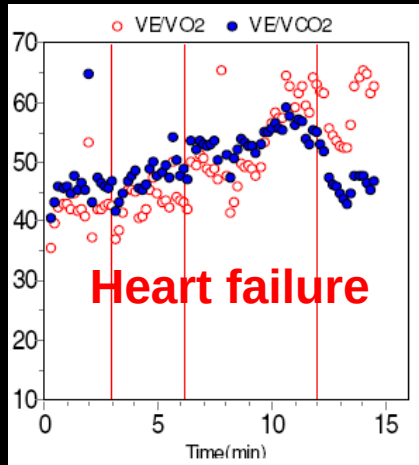
Ventilatory equivalents in the diagnosis of pulmonary vascular disease (PVD)



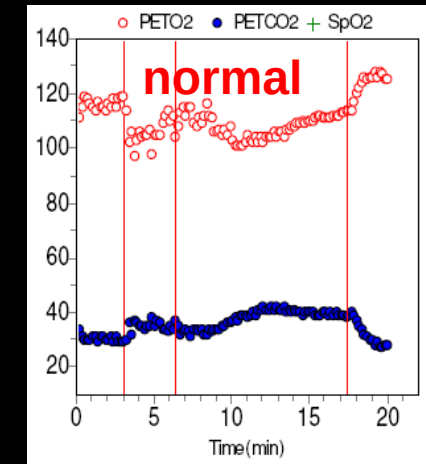
Pulmonary Ventilation-/Perfusion mismatch, reflected by ventilatory efficiency: VE/VCO2(left) and PETCO2 (right)



Ventilatory equivalents in the diagnosis of pulmonary vascular disease (PVD)



Pulmonary Ventilation-/Perfusion mismatch, reflected by ventilatory efficiency: VE/VCO₂(left) and PETCO₂ (right)



What does CPET show in Heart Failure?

Altered CPET parameters in Heart Failure

- Peak VO_2 ↓
- Anaerobic Threshold (VT_1) ↓
- Peak Oxygen Pulse (VO_2/HR) ↓
- Ventilatory Inefficiency (VE/VCO_2) ↑
- End-tidal CO_2 partial pressure ($\text{P}_{\text{ET}}\text{CO}_2$) ↓

Altered CPET parameters in Heart Failure

- Peak VO_2 ↓
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- Ventilatory Inefficiency (VE/VCO_2) ↑
- End-tidal CO_2 partial pressure ($\text{P}_{\text{ET}}\text{CO}_2$) ↓
- Oscillatory Breathing

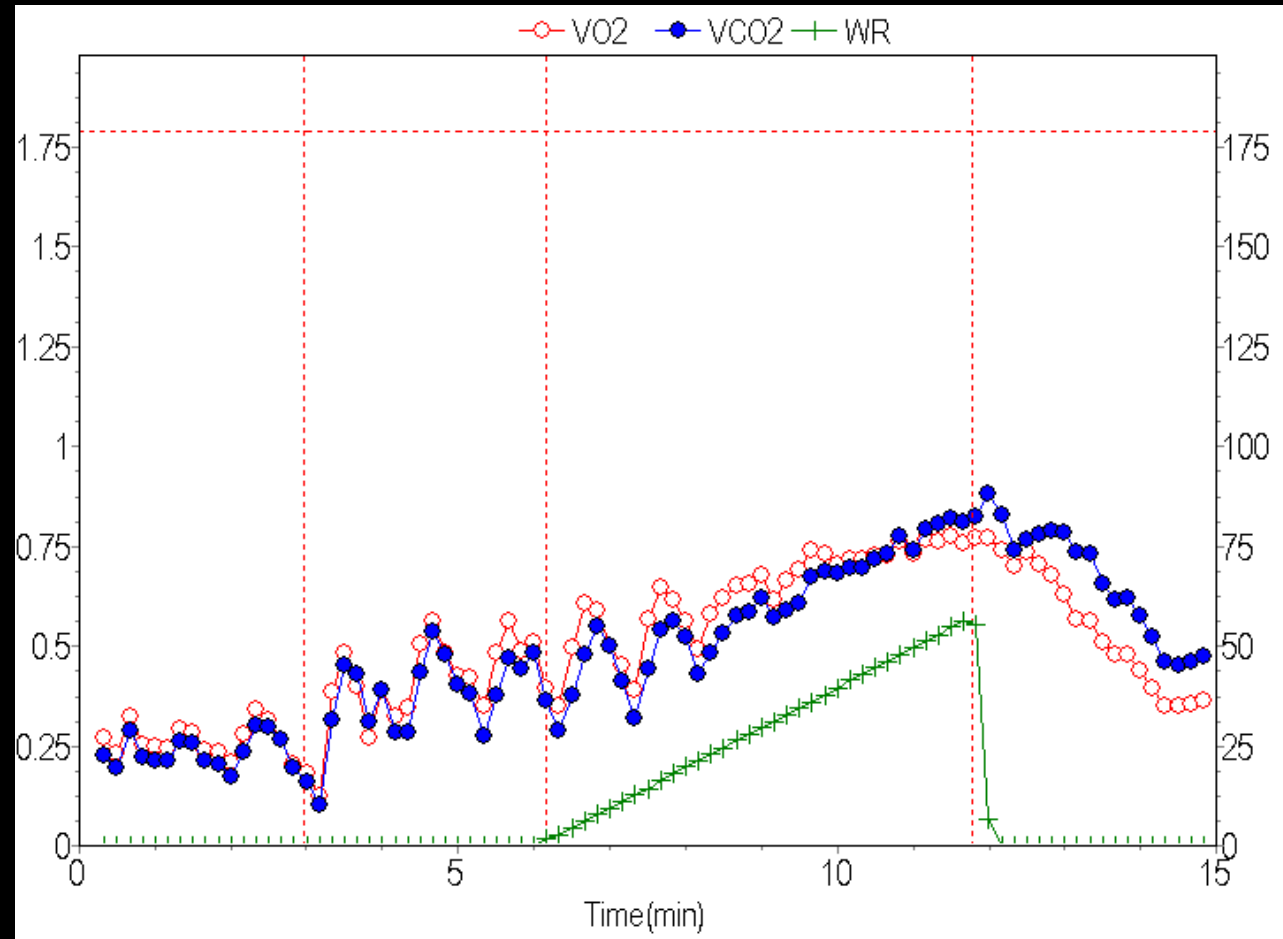
Clinical Case: Oscillatory Breathing

GV, 71J, male
168 cm, 78 kg
Ex-smoker
(30 Pack Years)

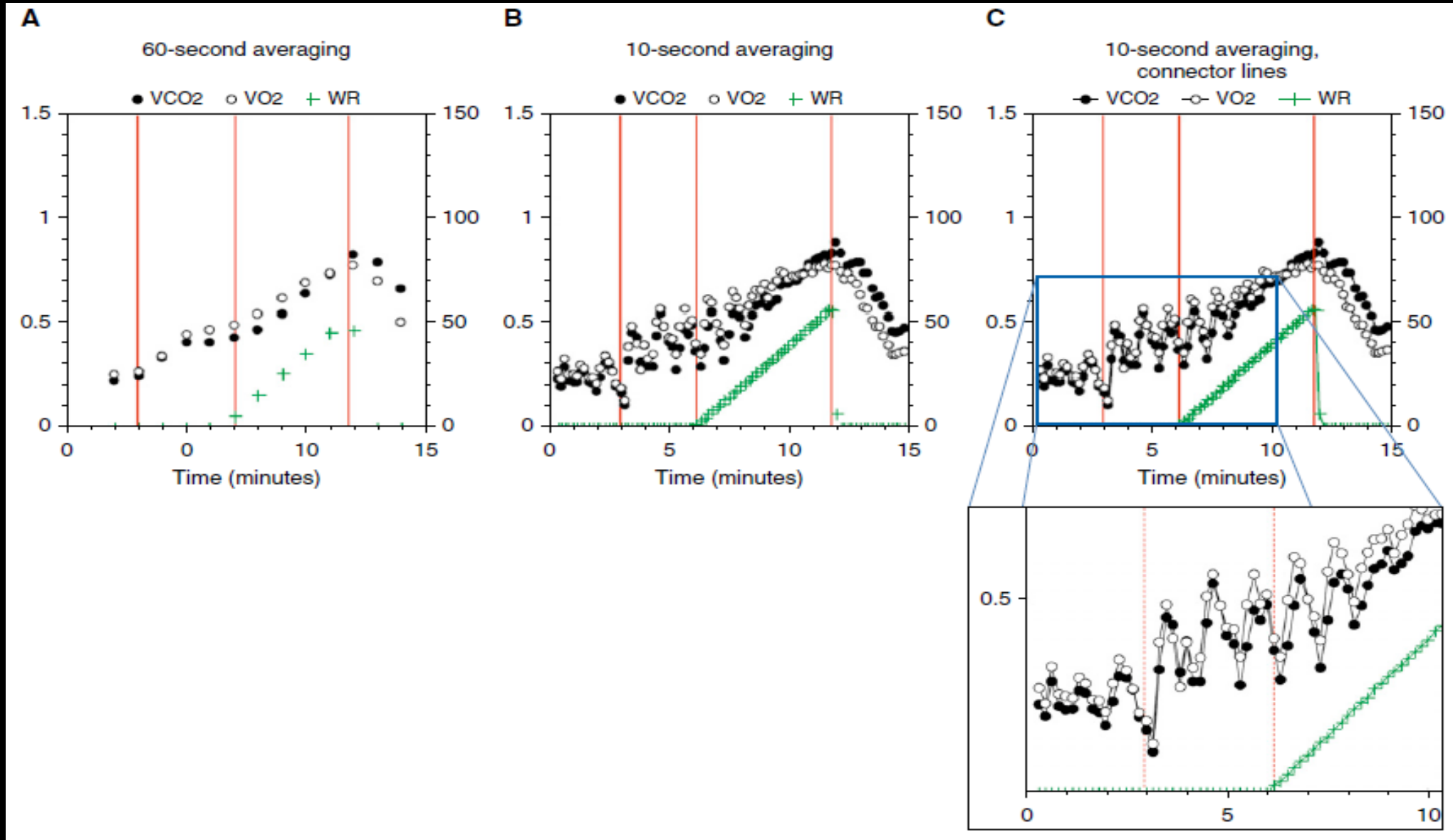
Ischemic
Cardiomyopathy

VC max 106,2% d.N.
FEV1: 113% d. N.
DLCO: 49 % d. N.

Peak VO₂: 0,8 L/min
AT: 0,65 L/min
VE/VCO₂@AT: 41
PETCO₂@AT: 29 mmHg



Oscillatory Breathing: Be careful with averaging



2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC

Authors/Task Force Members: Theresa A. McDonagh* (Chairperson) (United Kingdom), Marco Metra * (Chairperson) (Italy), Marianna Adamo (Task Force Coordinator) (Italy), Roy S. Gardner (Task Force Coordinator) (United Kingdom), Andreas Baumbach (United Kingdom), Michael Böhm (Germany), Haran Burri (Switzerland), Javed Butler (United States of America), Jelena Čelutkienė (Lithuania), Ovidiu Chioncel (Romania), John G.F. Cleland (United Kingdom), Andrew J.S. Coats (United Kingdom), Maria G. Crespo-Leiro (Spain), Dimitrios Farmakis (Greece), Martine Gilard (France), Stephane Heymans

ESC Guideline Recommendations

Cardiopulmonary exercise testing		
Cardiopulmonary exercise testing is recommended as a part of the evaluation for heart transplantation and/or MCS. ^{94–96}	I	C
Cardiopulmonary exercise testing should be considered to optimize prescription of exercise training. ^{94–96}	IIa	C
Cardiopulmonary exercise testing should be considered to identify the cause of unexplained dyspnoea and/or exercise intolerance. ^{94–96}	IIa	C

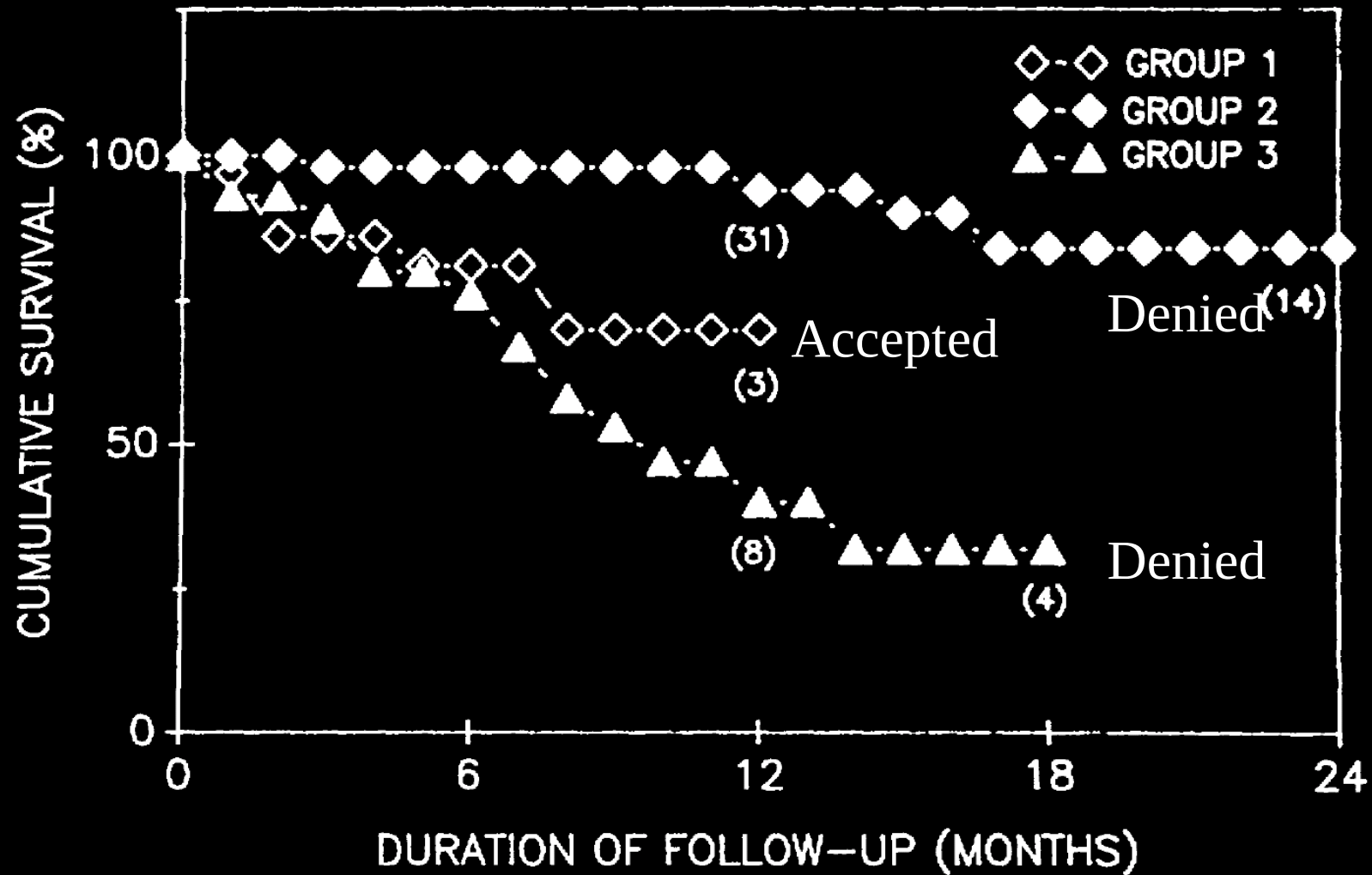
**Who should receive
heart transplantation or
mechanical cardiac support?**

Risikostratifizierung vor Herztransplantation

Erste Daten zur Risikostratifizierung anhand der peak VO_2 (1991)

Gruppe	Peak VO_2 (ml/min/kg)	Transplantation
1	< 14	Akzeptiert
2	≥ 14	Abgelehnt
3	< 14	Abgelehnt

Risikostratifizierung vor Herztransplantation

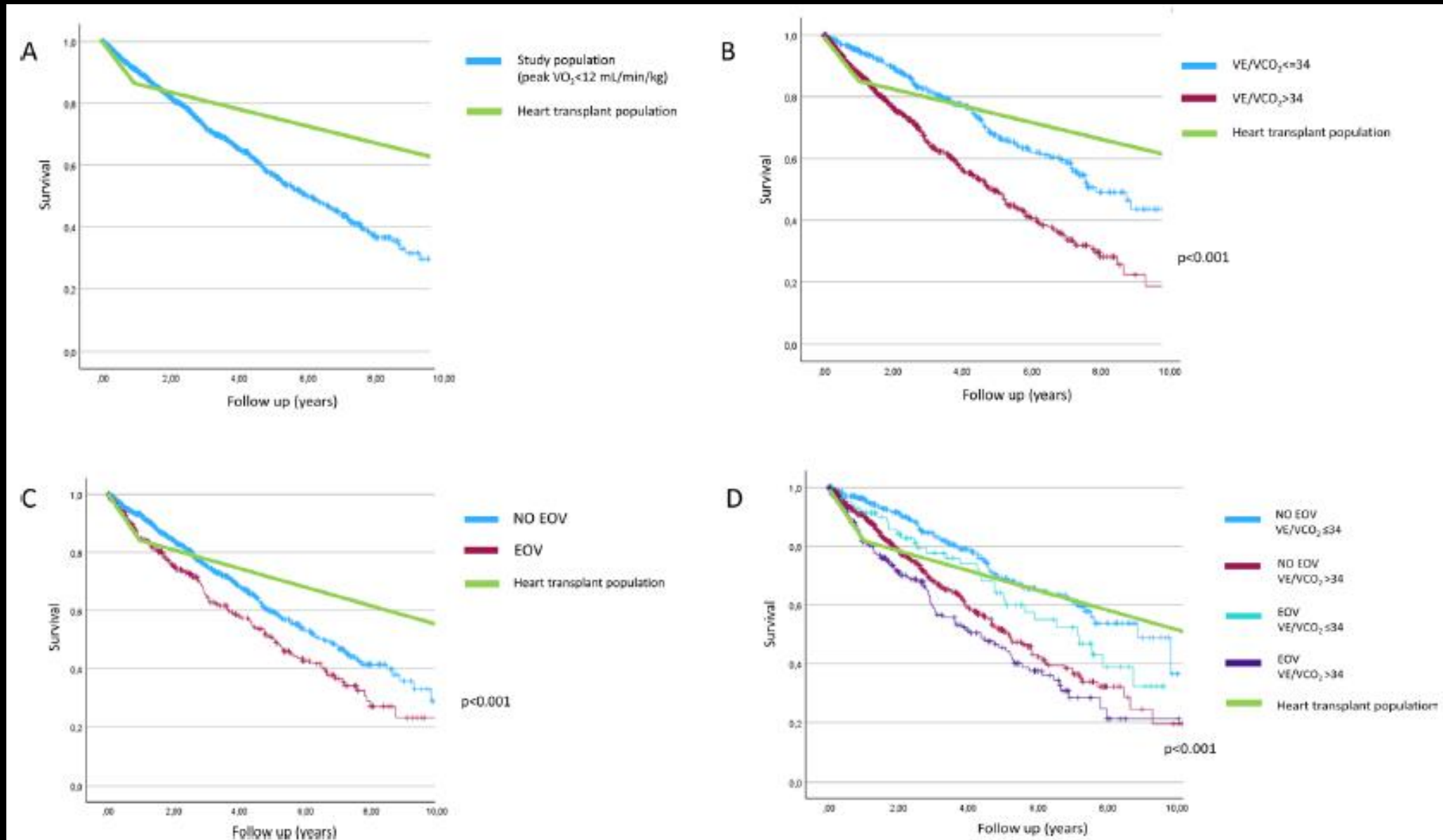


Spiroergometrie für die Evaluation für eine Herztransplantation

ISHLT-Leitlinien (2024):

Table 4 Summary of CPET Parameters Supporting Transplant Listing in Different Populations	
Patient population	Parameter supporting transplant listing
On beta-blocker ^{63–67}	Lower peak VO_2 cutoff is supportive of transplant listing, generally ≤ 12 ml/kg/min
Off beta-blocker ^{67,68}	Higher peak VO_2 may be considered supportive of transplant listing, generally ≤ 14 ml/kg/min
Patients with obesity ($\text{BMI} \geq 30$ kg/m ²) ⁶⁹	Peak VO_2 adjusted for lean body mass ≤ 19 ml/kg/min
All, especially if submaximal CPET ^{70–75}	VE/VCO_2 slope > 35
Women or patients ≤ 50 or ≥ 70 years ^{76–78}	Peak $\text{VO}_2 \leq 50\%$ predicted
Abbreviations: BMI, body mass index; CPET, cardiopulmonary exercise test; VE/VCO_2 , the minute ventilation/carbon dioxide production. Maximal CPET: respiratory exchange ratio (RER) > 1.05 and reaching anaerobic threshold. ⁷⁹	

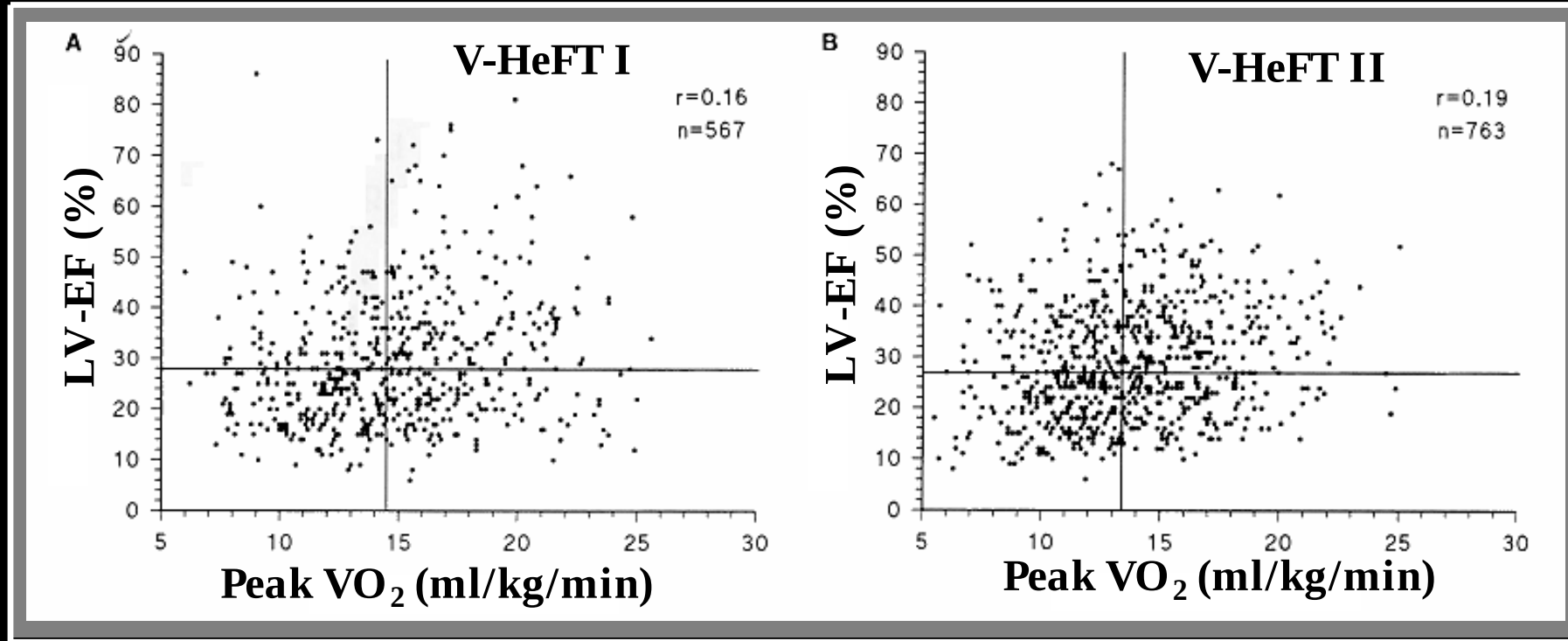
Risk Stratification for heart transplant: Peak VO_2 too simple?



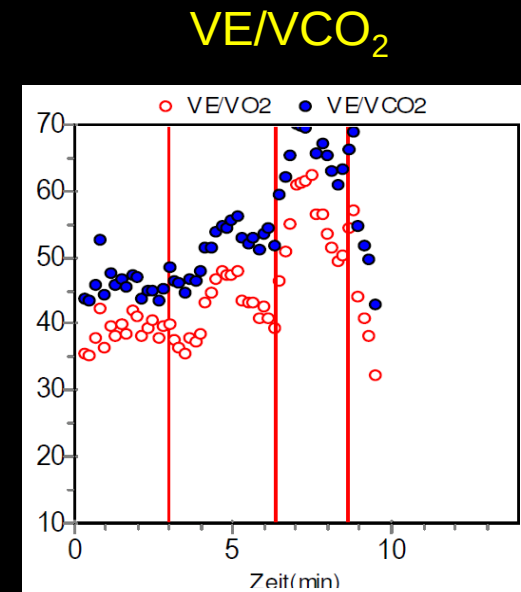
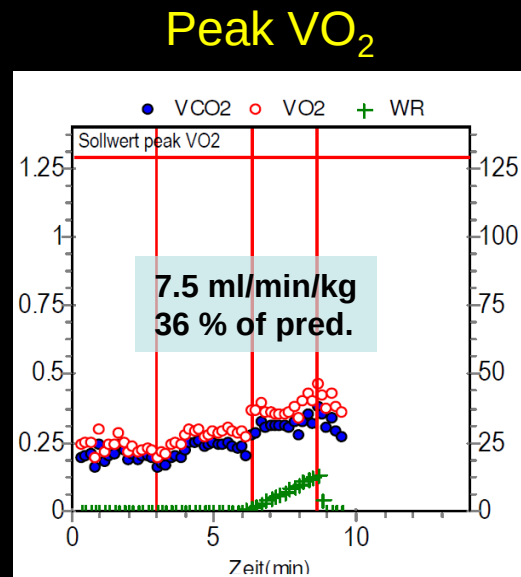
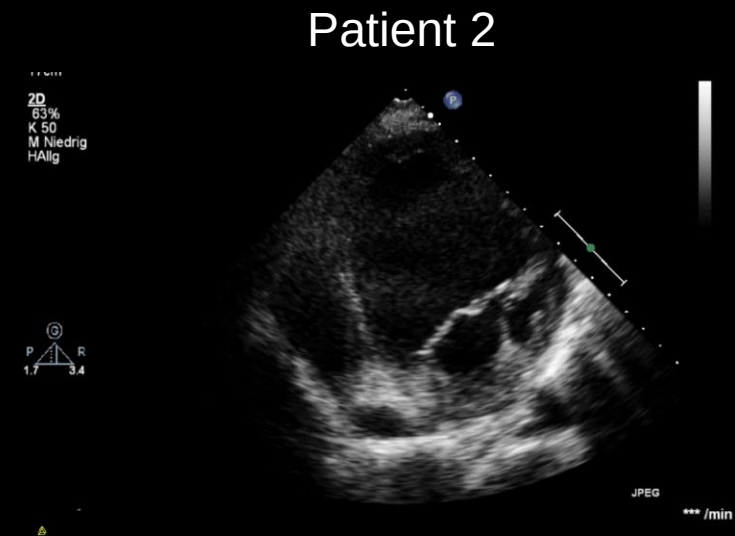
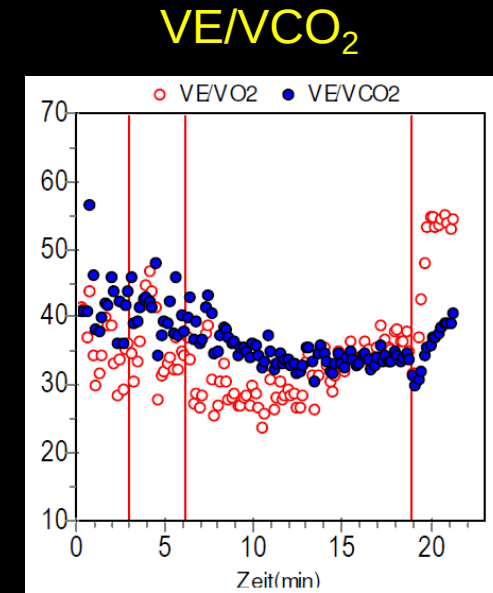
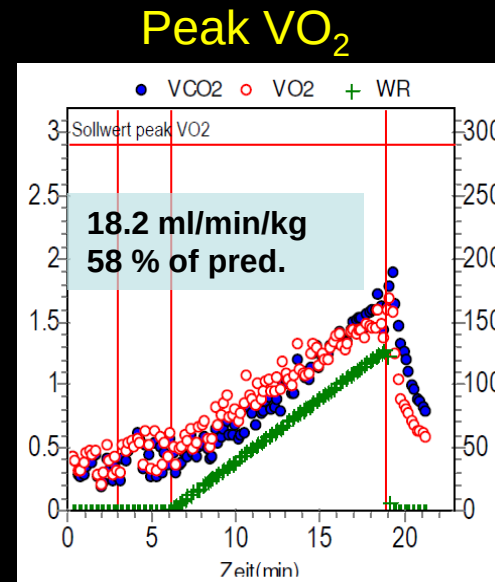
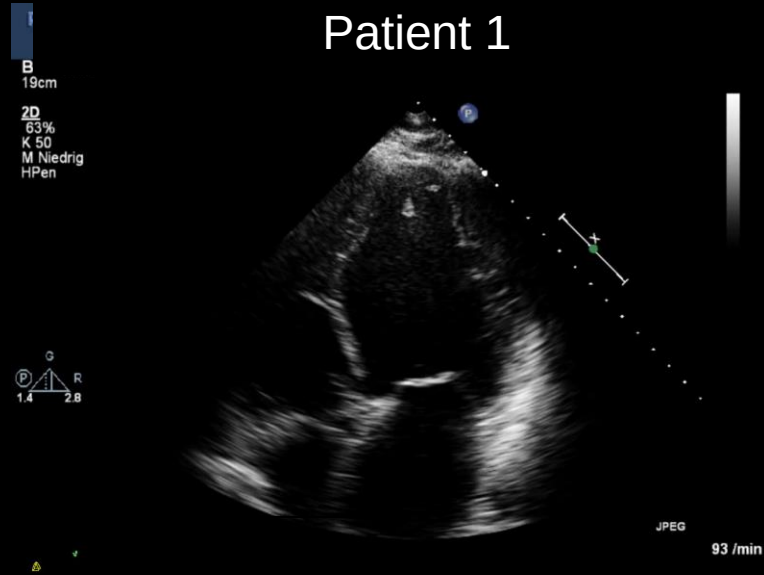
From: Azar M et al. Heart 2026

Risk stratification

Correlation between maximal oxygen uptake and left ventricular ejection fraction



Which patient is of higher risk?



Guideline Statements



Clinical Recommendations for Cardiopulmonary Exercise Testing Data Assessment in Specific Patient Populations

Marco Guazzi, Volker Adams, Viviane Conraads, Martin Halle, Alessandro Mezzani, Luc Vanhees, Ross Arena, Gerald F. Fletcher, Daniel E. Forman, Dalane W. Kitzman, Carl J. Lavie and Jonathan Myers

Risk Stratification in Heart Failure

Primary CPX variables				
VE/VCO ₂ slope		Peak V _{O₂} ^a	EOV	P _{ET} CO ₂
Ventilatory class I VE/VCO ₂ slope <30.0	Weber class A Peak V _{O₂} >20.0 mL O ₂ •kg ⁻¹ •min ⁻¹	Not present		Resting P _{ET} CO ₂ ≥33.0 mmHg
Ventilatory class II VE/VCO ₂ slope 30.0–35.9	Weber class B Peak V _{O₂} = 16.0–20.0 mL O ₂ •kg ⁻¹ •min ⁻¹			3–8 mmHg increase during ET
Ventilatory class III VE/VCO ₂ slope 36.0–44.9	Weber class C Peak V _{O₂} = 10.0–15.9 mL O ₂ •kg ⁻¹ •min ⁻¹	Present		Resting P _{ET} CO ₂ <33.0 mmHg
Ventilatory class IV VE/VCO ₂ slope ≥45.0	Weber class D Peak V _{O₂} <10.0 mL O ₂ •kg ⁻¹ •min ⁻¹			<3 mmHg increase during exercise
Standard ET variables				
Haemodynamics		ECG		HRR
Rise in systolic BP during ET		No sustained arrhythmias, ectopic foci, and/or ST segment changes during ET and/or in recovery		>12 beats at 1 min recovery
Flat systolic BP response during exercise		Altered rhythm, ectopic foci, and or ST segment changes during ET and/or in recovery: did not lead to test termination		≤12 beats at 1 min recovery
Drop in systolic BP during ET		Altered rhythm, ectopic foci, and or ST segment changes during ET and/or in recovery: led to test termination		
Patient reason for test termination				
Lower extremity muscle fatigue		Angina		Dyspnoea

MECKI score

**Metabolic Exercise test data
combined with Cardiac and Kidney
Indexes**



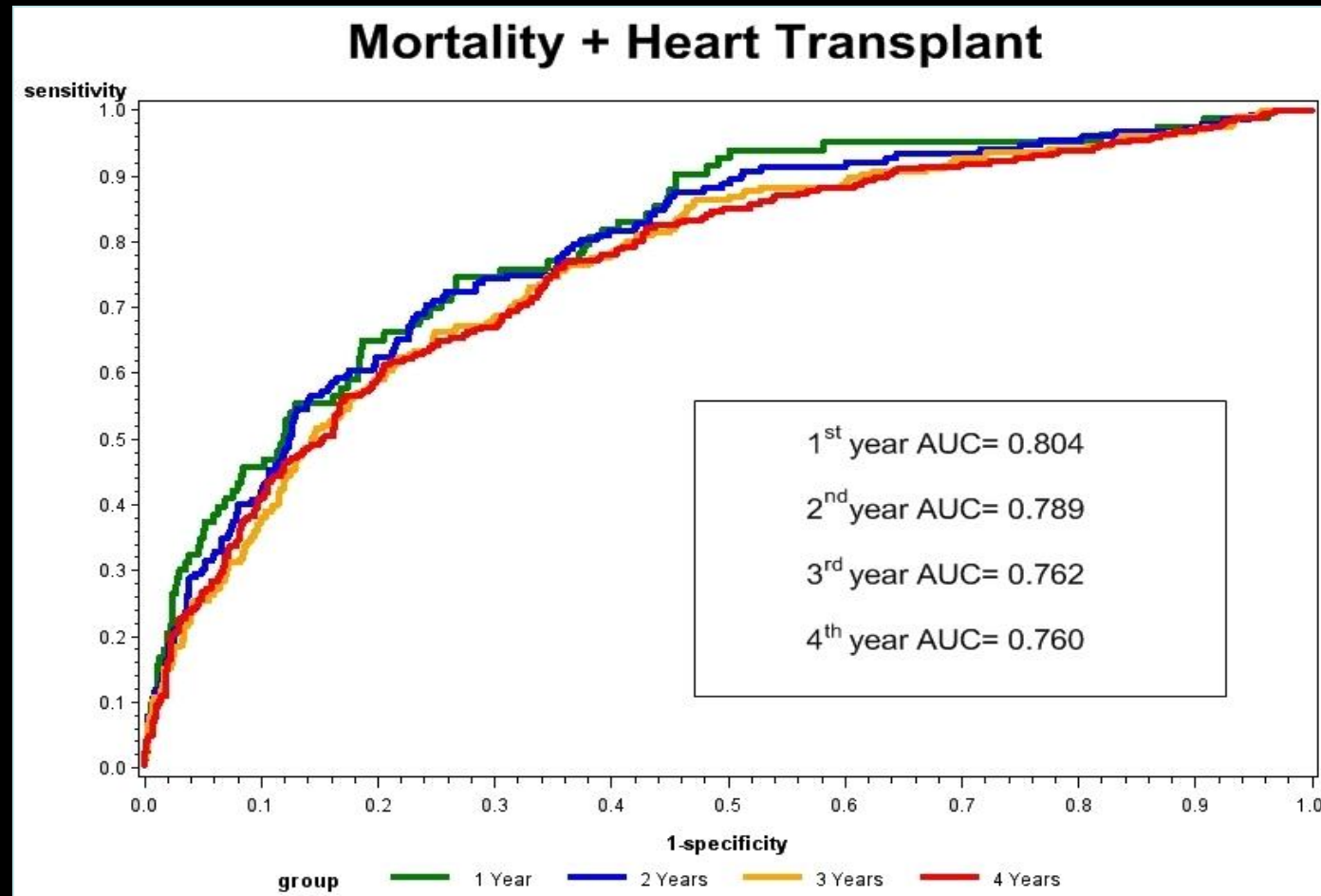
Metabolic exercise test data combined with cardiac and kidney indexes, the MECKI score: A multiparametric approach to heart failure prognosis

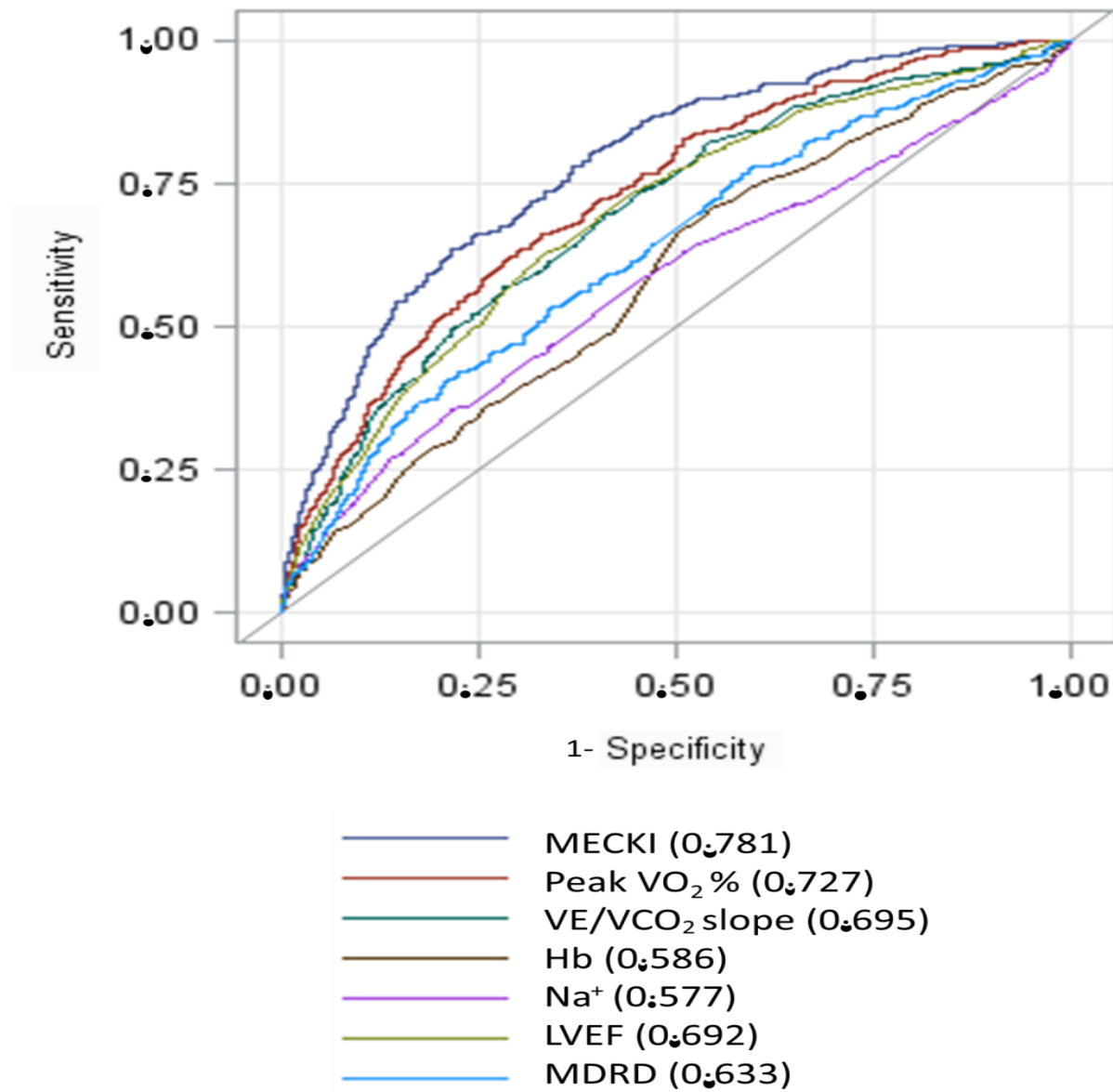


Parameter	Pr > ChiSq	Hazard	95% Hazard		selection	reconfirmation
			Ratio Confidence			
			Ratio	Limits		
Peak VO ₂ (% pred)	<.0001	0.708	0.614	0.816	84.0%	93.5%
VE/VCO ₂ Slope	<.0001	1.291	1.165	1.431	85.0%	95.3%
Hb (g/dl)	0.0008	0.827	0.74	0.924	85.5%	94.2%
Na ⁺ (mmol/L)	<.0001	0.796	0.719	0.881	96.5%	92.7%
LVEF (%)	<.0001	0.699	0.61	0.802	90.0%	93.9%
MDRD (mL/min)	<.0001	0.758	0.673	0.854	66.0%	81.1%

	LVEF (%)	Peak VO ₂ (%)	Na ⁺ (mmol/L)	Hb (g/dL)	MDRD (mL/min)	VE/VCO ₂ slope
< 5%	36.74 ± 7.35	61.92 ± 14.16	140.4 ± 3.1	13.9 ± 1.5	77.09 ± 20.91	28.67 ± 4.6
5 -10	29.28 ± 7	51.55 ± 11.29	139.7 ± 3.2	13.4 ± 1.6	68.89 ± 20.26	32.62 ± 5.13
10 -15	26.88 ± 7.08	45.6 ± 10.25	138.8 ± 3.2	13.3 ± 1.5	62.94 ± 20.77	34.86 ± 5.45
> 15%	23.75 ± 6.77	38.2 ± 9.94	137.7 ± 3.7	13.0 ± 1.64	56.43 ± 20.21	41.98 ± 7.96

Metabolic exercise test data combined with cardiac and kidney indexes, the MECKI score: A multiparametric approach to heart failure prognosis





MECKI Score - Cardiologico Monzi

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https://www.cardiologicomonzino.it/en/mecki-score/

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Research for care

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ABOUT MONZINO

CLINICAL ACTIVITIES

PATIENT SERVICES

RESEARCH

PEAK VO_2 (%PRED)

50

VE/ VCO_2 (SLOPE)

45

HEMOGLOBIN (G/DL)

13

NA^+ (MMOL/L)

140

LVEF (%)

30

MDRD (ML/MIN)

80

CALCULATE

11.44% risk of cardiovascular death or heart transplant within 2 years

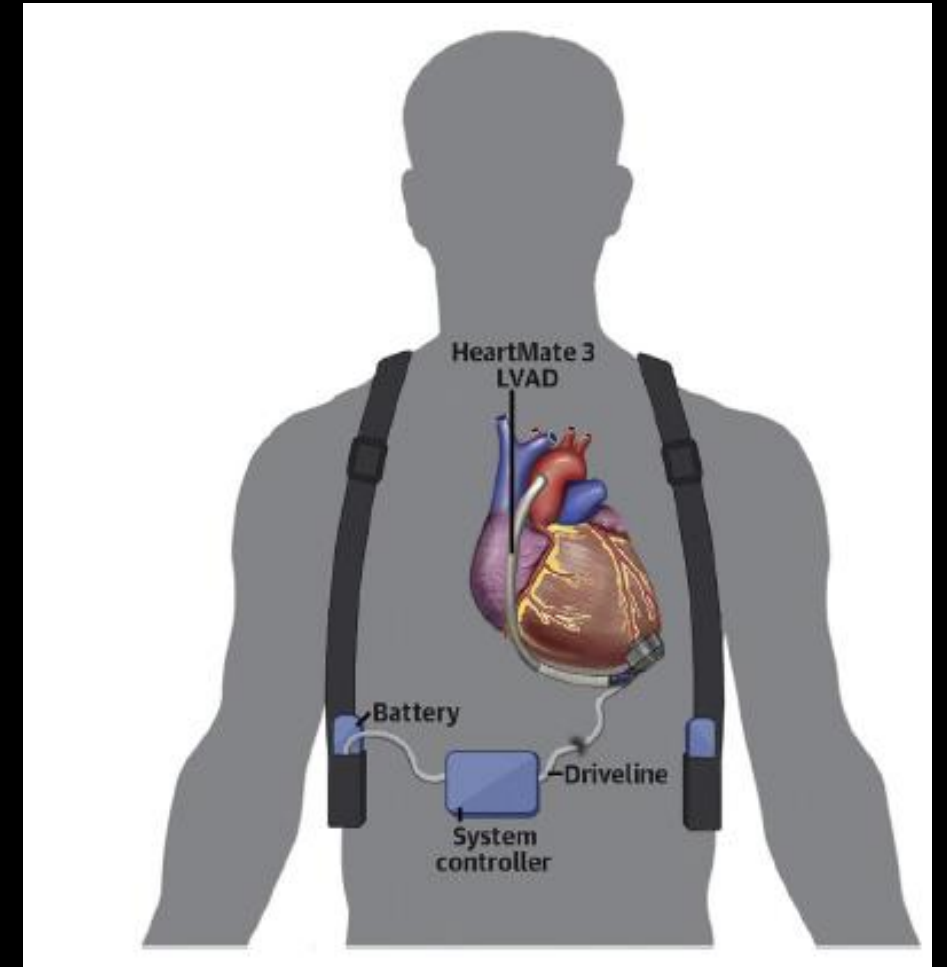
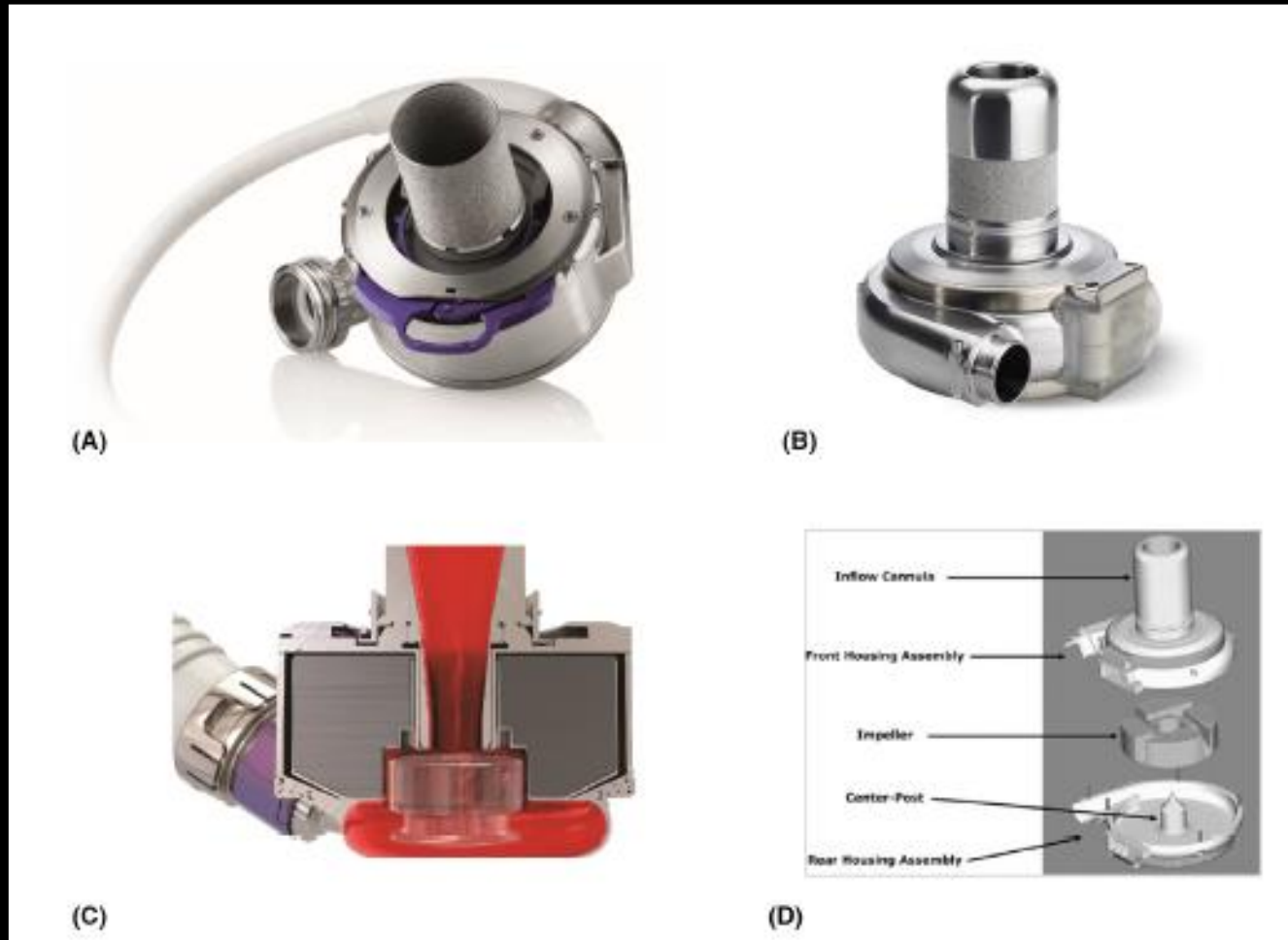
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MECKI SCORE AT PREVIOUS VISIT (%)

Accessed at <https://www.cardiologicomonzino.it/en/mecki-score>

LVAD weaning

Left ventricular assist device (LVAD)



Ischemia

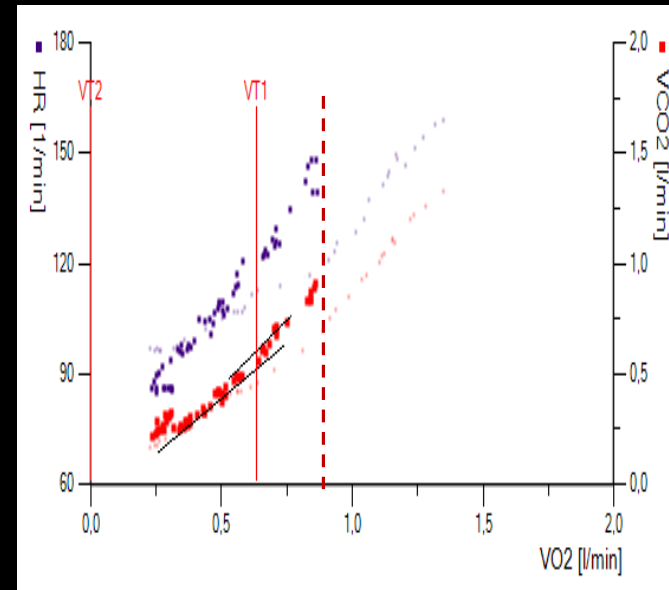
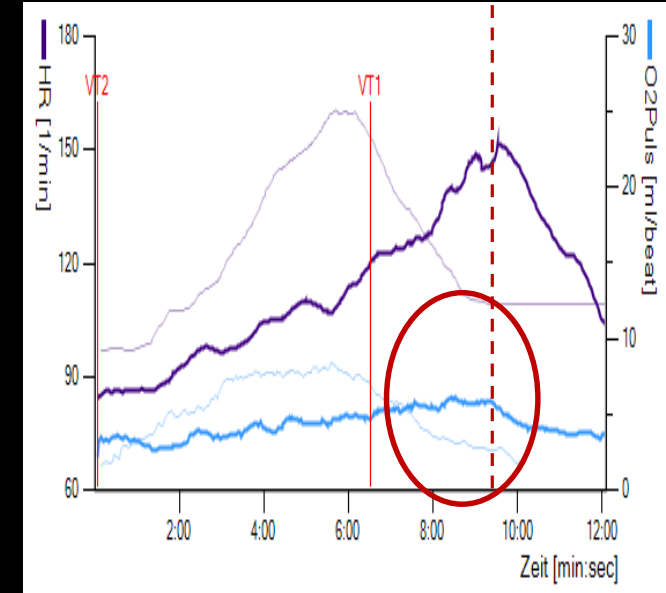
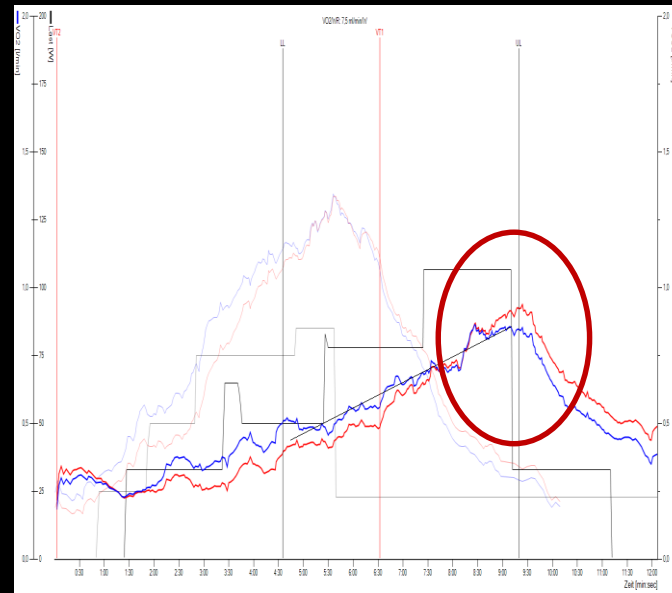
Clinical Case:

66Y, female
165 cm, 65 kg
non-smoker

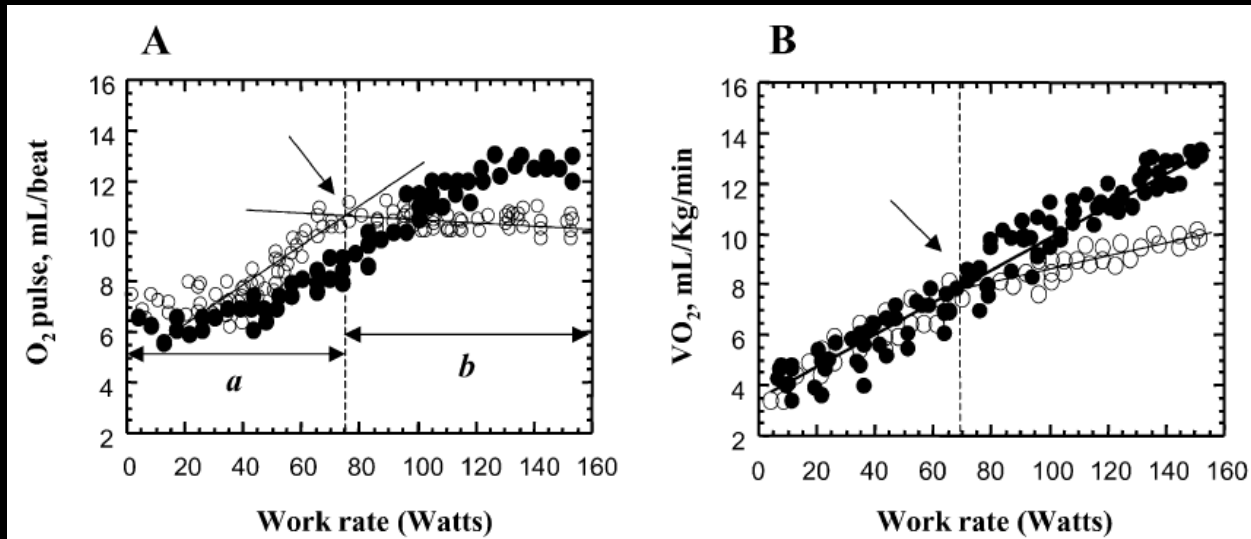
Symptoms:

Progressive dyspnea
on exertion

Peak VO_2 : 0.9 L/min
 VT_1 : 0.55 L/min (46 % peak VO_2)
Nadir VE/VCO_2 : 39
Peak PETCO_2 : 32 mmHg



CPET for detection of myocardial ischemia



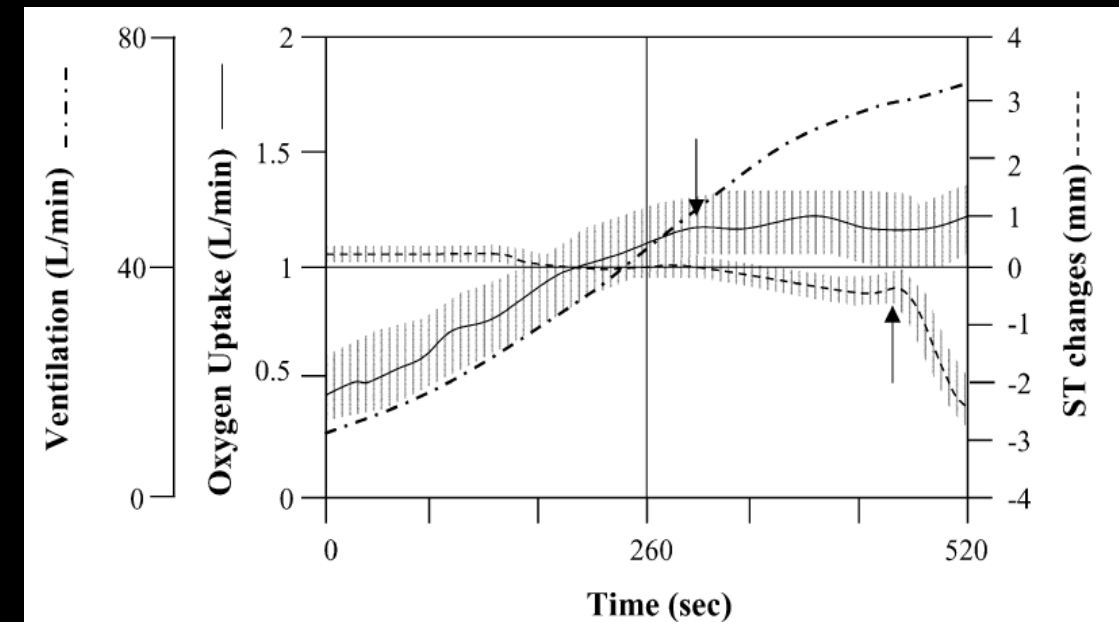
	Stress ECG	CPET
Sensitivity	0.46	0.87
Specificity	0.66	0.74
Positive predictive value	0.76	0.88
Negative predictive value	0.35	0.72

n=202: 173 men, 29 women

Gold standard: SPECT myocardial scintigraphy

Exclusion of patients with heart failure, anemia and respiratory disease

From: Bellardinelli R et al. Eur Heart J 2003.



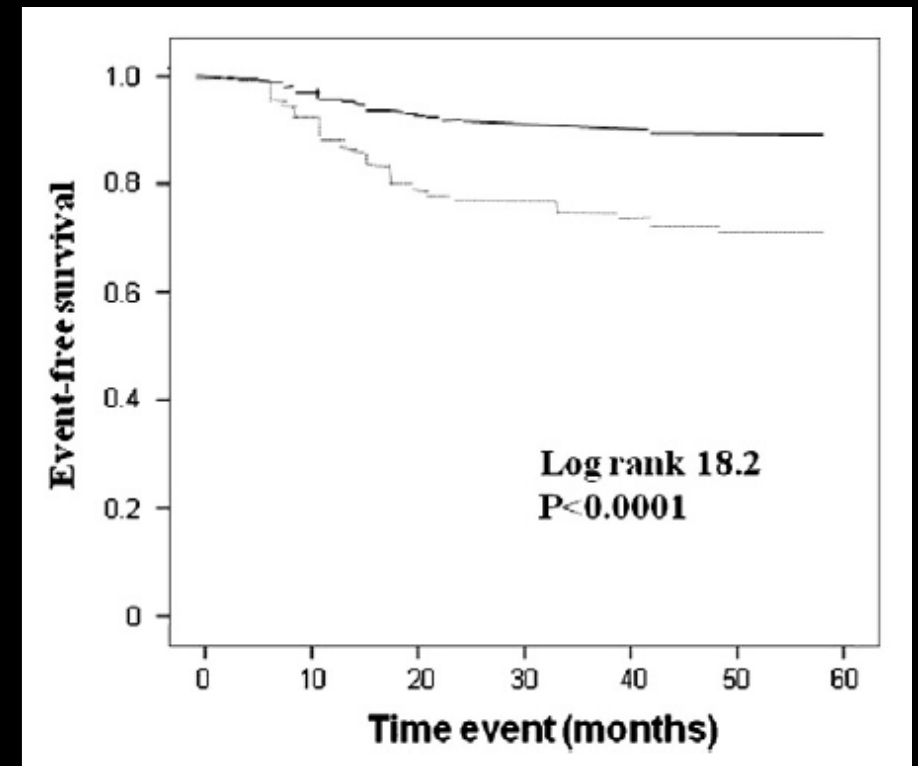
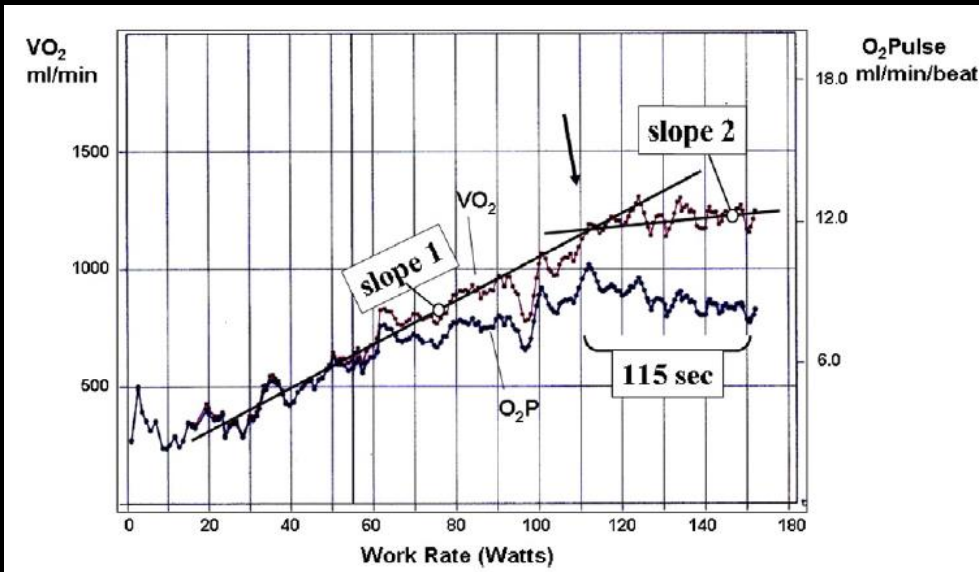
CPET for detection of coronary artery disease in patients with angina

n=144

Gold standard: Coronary angiography

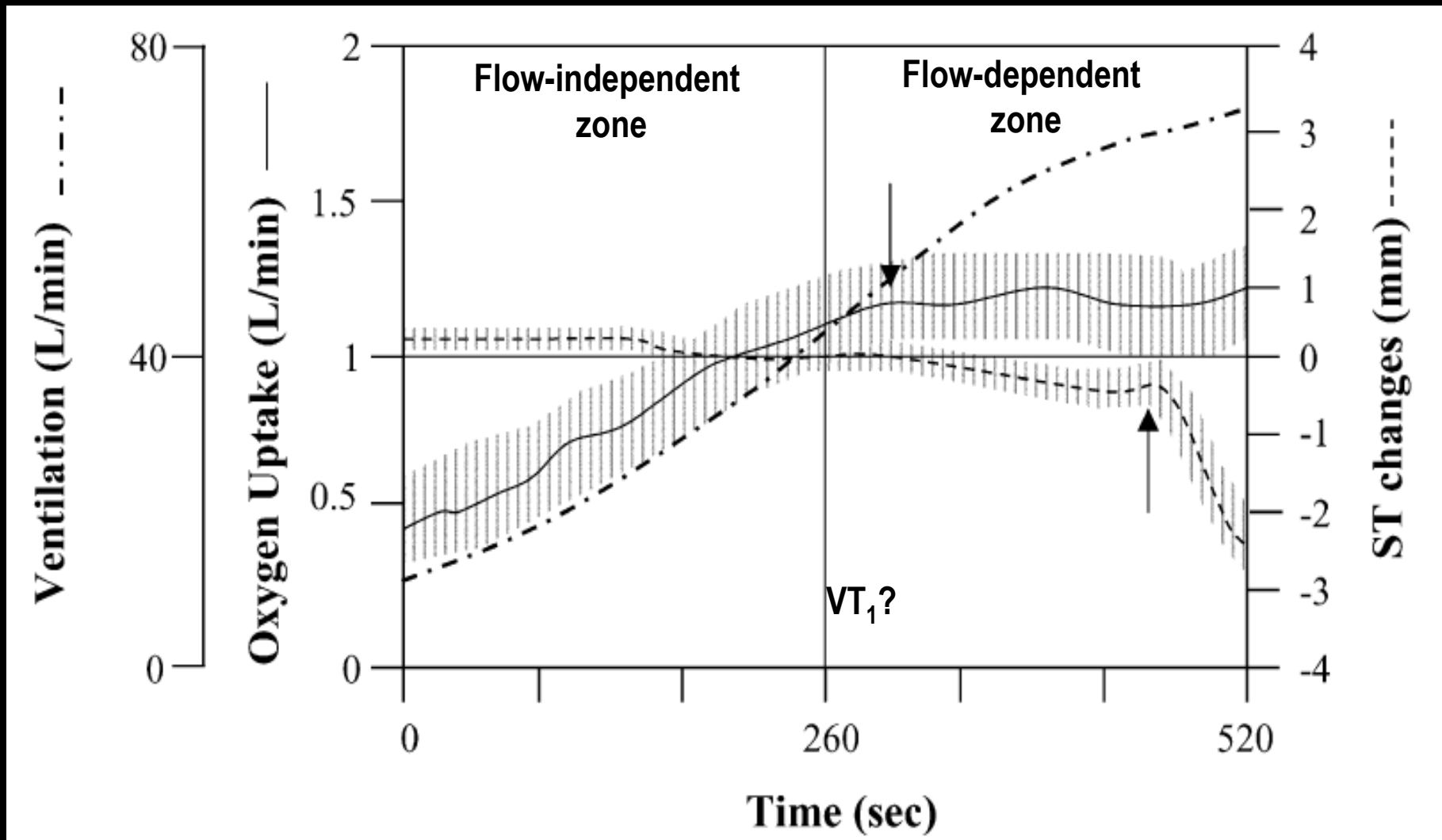
Exclusion of patients with heart failure, anemia and respiratory disease

	Stress ECG low	Stress ECG intermediate	Stress ECG high	CPET low	CPET intermediate	CPET high
Positive predictive value	0.20	0.42	0.54	0.35	0.60	0.84



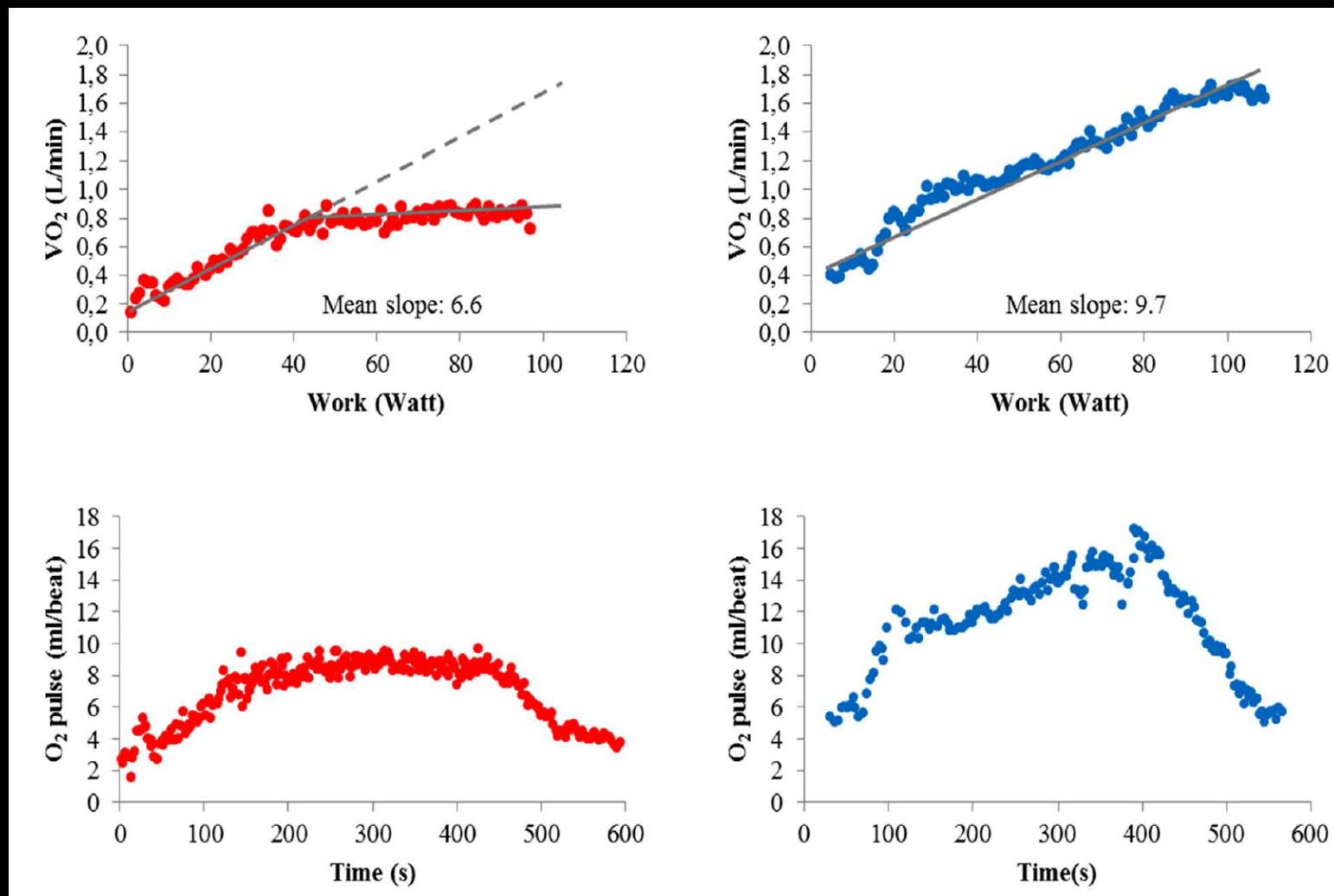
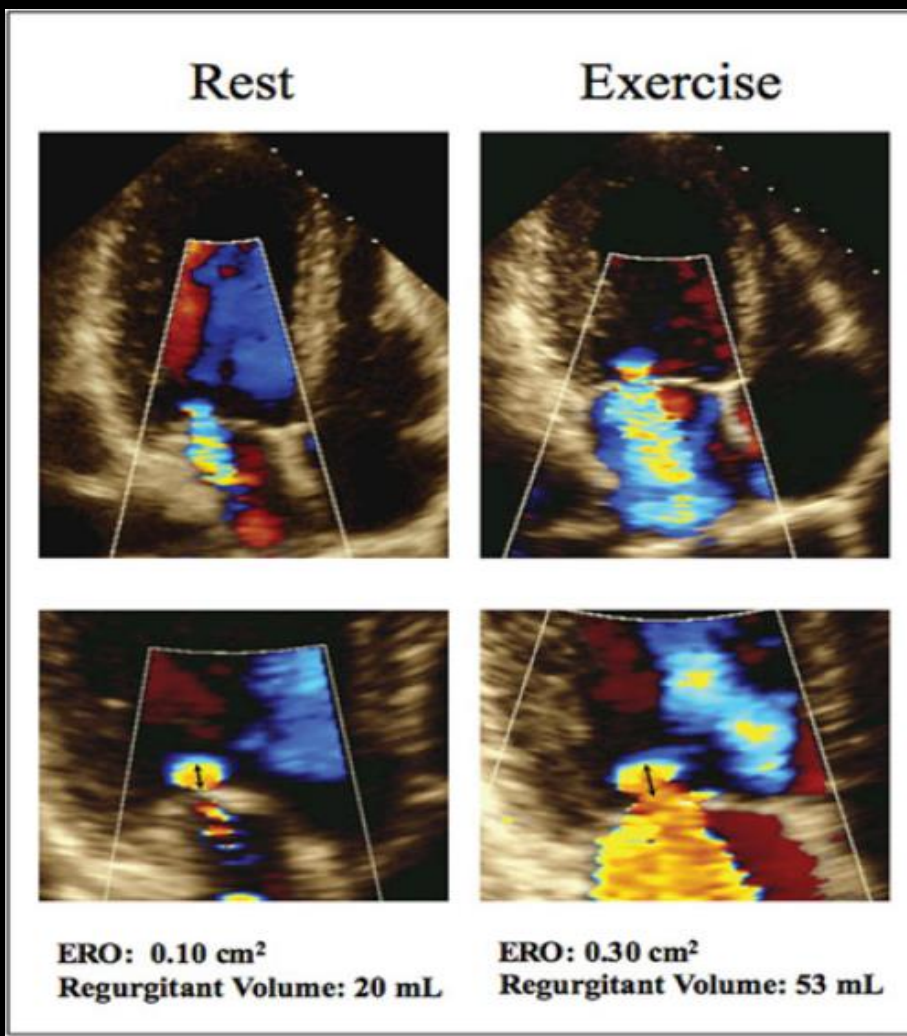
From: Bellardinelli R et al. Int J Cardiol 2014.

CPET for detection of myocardial ischemia

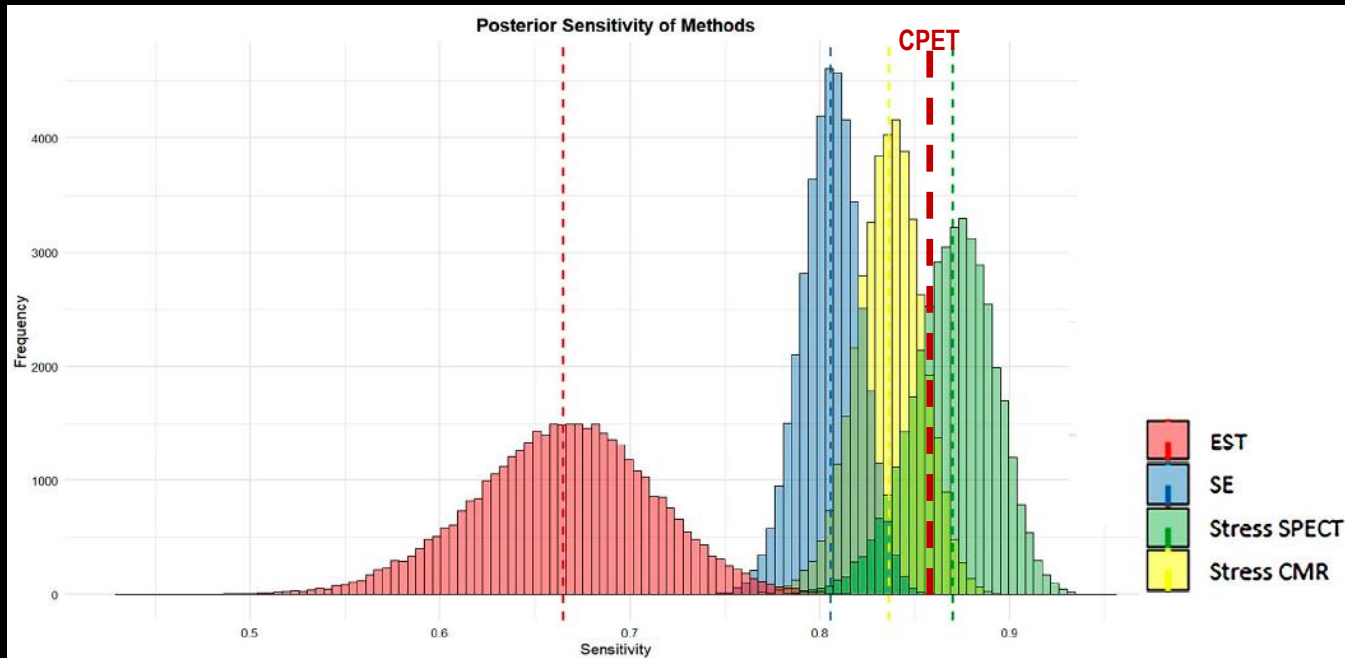


From: Bellardinelli R et al. Eur Heart J 2003.

Gas exchange abnormalities in dynamic mitral valve insufficiency

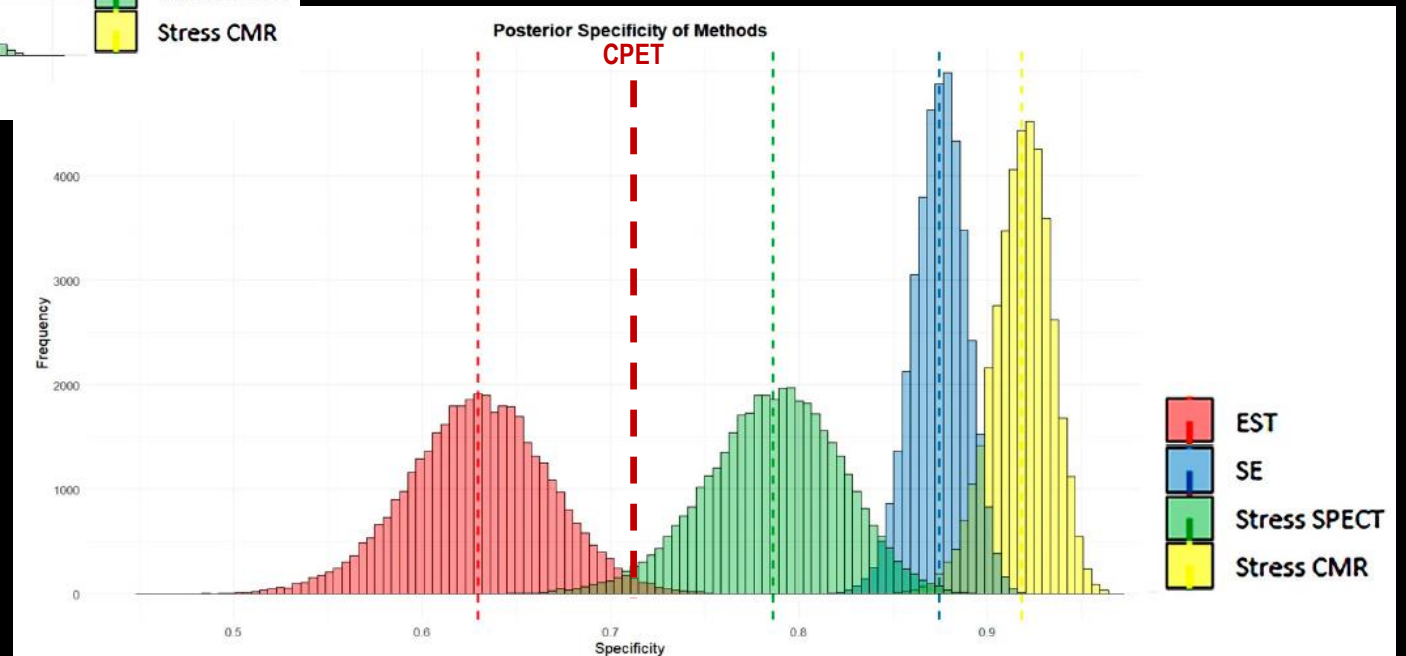


CPET for detection of coronary artery disease in patients with angina



104 studies

n=16.824 patients



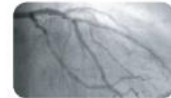
From: Sonaglioni A et al. J Clin Med 2025.

Detection of coronary artery disease: State-of-the-art

Clinical likelihood of obstructive CAD^a

Appropriate first-line test for suspected CCS

Invasive coronary angiography



Functional imaging

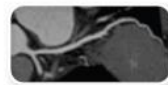


PET/SPECT

CMR

Stress ECHO

CCTA



OR

Functional imaging



PET/SPECT

CMR

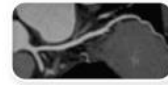
Stress ECHO

Adjust the clinical likelihood



OR

CCTA

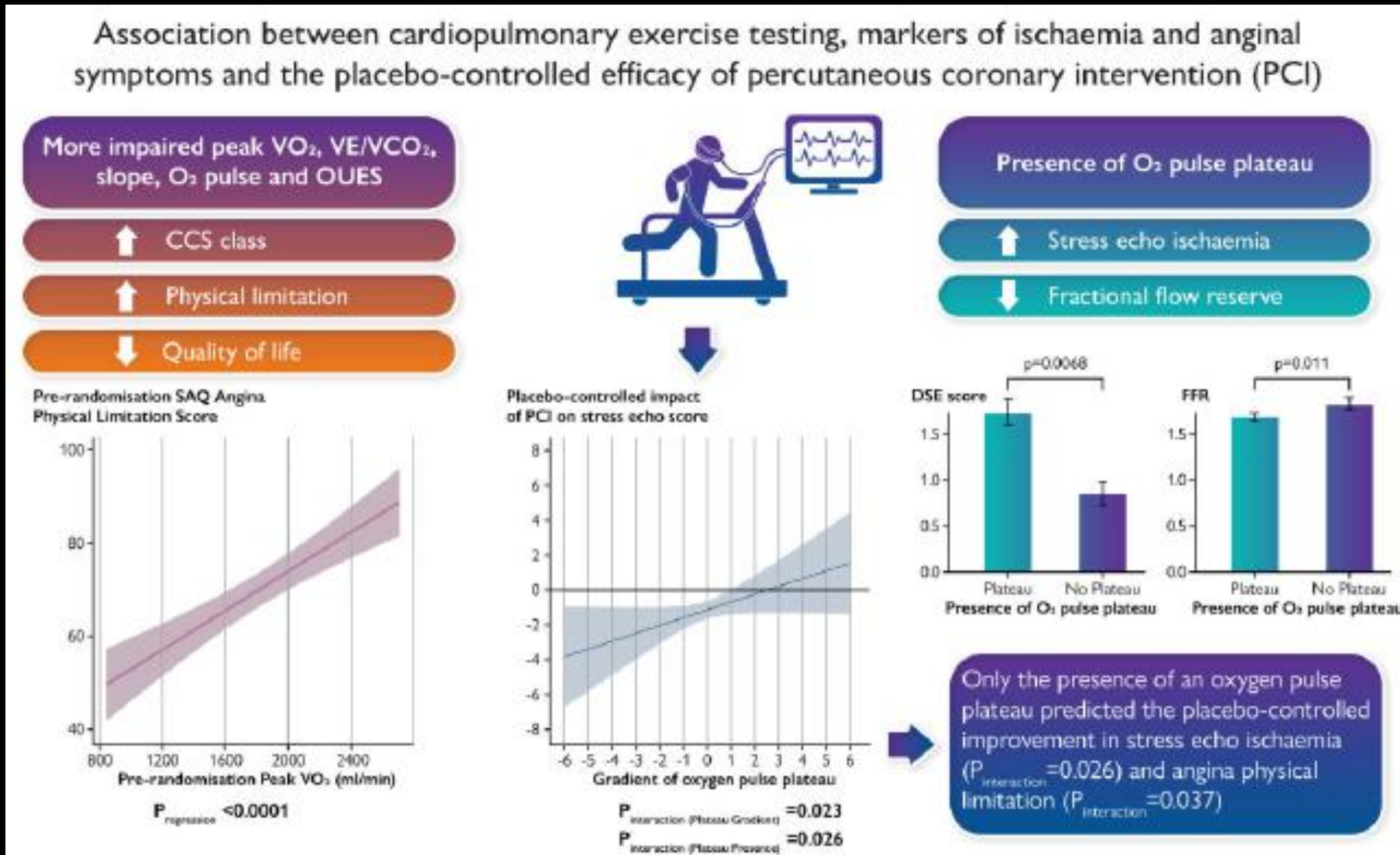


Defer further testing



Test	Clinical Use	Recommendations (ESC 2024) [6]
EST	Low pre-test likelihood (5–15%) of CAD; assessment of symptoms, arrhythmias, and BP response.	May be used to reclassify patients to very low risk ($\leq 5\%$) when negative. Recommended for functional capacity and symptom evaluation (Class I C). May be used when imaging is unavailable (Class IIb B).
SE	Moderate to high pre-test likelihood (15–85%) of CAD; evaluation of myocardial ischemia, arrhythmias, and microvascular dysfunction.	Recommended to diagnose ischemia and estimate MACE risk (Class I B). Doppler CFR and myocardial contrast agents may be used to enhance diagnostic and prognostic value (Class IIb B and Class I B).
Stress myocardial SPECT	Moderate to high pre-test likelihood (15–85%) of CAD; diagnosis and quantification of ischemia and/or scarring.	Recommended for diagnosis and risk assessment in moderate-to-high risk patients (Class I B). CACs should be measured when SPECT/PET is used (Class I B). Prefer PET when available
Stress CMR	Moderate to high pre-test likelihood (15–85%) of CAD; comprehensive assessment of perfusion, function, and viability.	Recommended for diagnosis of ischemia and scarring, and risk stratification (Class I B). Use in cases needing additional information beyond perfusion.

Detection of coronary artery disease: State-of-the-art





Thank you for your attention!