VCU Health
Pauley Heart Center

"Discerning the Cause(s) of Exercise Intolerance – the Role of Cardiopulmonary Exercise Testing"

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Faculty Disclosures

- None.

Overview/Learning Objectives

- Describe the physiologic principles underlying cardiopulmonary exercise testing (CPET), including oxygen consumption, ventilatory efficiency, and cardiovascular and pulmonary responses to exercise

- Review/identify the key variables obtained during cardiopulmonary exercise testing

- Apply CPET results to clinical decision-making, including risk stratification, diagnosis, prognosis, and guidance of therapeutic interventions in patients with cardiovascular and pulmonary disease

Educational Need/Practice Gap

Gap = Cardiopulmonary exercise testing (CPET) is a diagnostic tool that can be used in evaluating unexplained dyspnea, exercise intolerance, heart failure severity, and perioperative risk

- This particular tool is not currently available at Med Center Health

Need = The issue/problem that underlies the practice gap

- Clinicians are not trained to interpret or utilize multiparametric responses in CPET
- This leads to low utilization or recognition of CPET in current practice.

Expected Outcome

What is the desired change/result in practice resulting from this educational intervention?

- Cardiopulmonary exercise testing will be utilized more frequently to discern causes of exercise intolerance.
- Understanding of additional CPET variables to elucidate organ-limiting systems.

Case Study 1 - Dyspnea on Exertion

53yoF referred for CPET due to “dyspnea out of proportion to PFTs, exertional dyspnea” by outside pulmonologist

PMH: emphysema, GERD, hilar lymphadenopathy, h/o Covid pneumonia, h/o aspiration pneumonia-started on supplemental oxygen

Social Hx: 30-pack year smoker – quit 4-years ago; participates in Cross-Fit 4xweek

Medications: Anoro-Ellipta™, escitalopram, omeprazole, Vitamin D2

PE: 132/79, HR=72, RR=20, BMI= 41.3

Labs/ Diagnostic Studies: Hgb= 15.1 g/dL
CT Chest – moderate upper lobe centrilobular and paraseptal emphysema. Bronchial wall thickening representing smoking-related chronic bronchitis
Endobronchial ultrasound (EBUS) with fine-needle aspiration- Negative
Transthoracic Echo – LVEF= 55-60%, NL diastolic function, NL left atrial pressure, no evidence of cardiac shunting
Outside PFTs – Spirometry “normal”; DLCO= 69%

Case 2 – Exercise Intolerance with history of PHTN

76yo Male referred by Pulmonologist for CPET to evaluate progressive exercise intolerance with a history of Pulmonary Hypertension

- PMH: PHTN (RVSP= 61 mmHg), LVEF=60%, permanent afib/flutter, s/p AVN ablation, pacemaker, OSA
- Medications: apixaban, atorvastatin, lisinopril
- Pre-test Considerations:
  - 30 pack-year smoking history (quit 31 years ago), BMI=27, Hgb= 12.2 g/dL, PPM settings: VVIR, 99.9% V-paced

Dyspnea

“a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity,”

Exertional dyspnea - “the perception of respiratory discomfort that occurs for an activity level that does not normally lead to breathing discomfort”

“derives from interactions among multiple physiological, psychological, social, and environmental factors, and may induce secondary physiological and behavioral responses,”

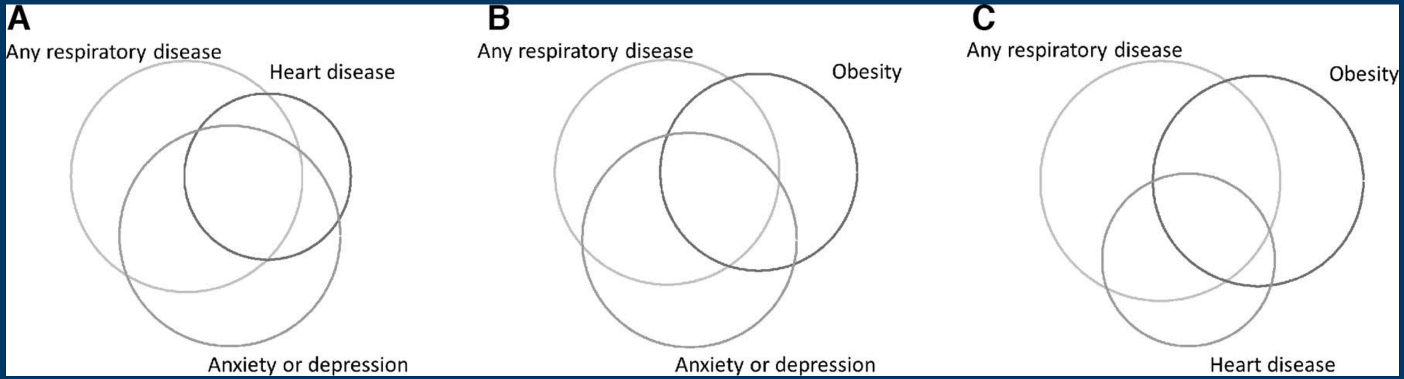
Parshall MB, Am J Respir Crit Care Med, 2012
Laviolette L, Eur Respir J, 2014

Prevalence of Dyspnea (SOB; Breathlessness)

~10% - 25% of middle age/older individuals in the general population

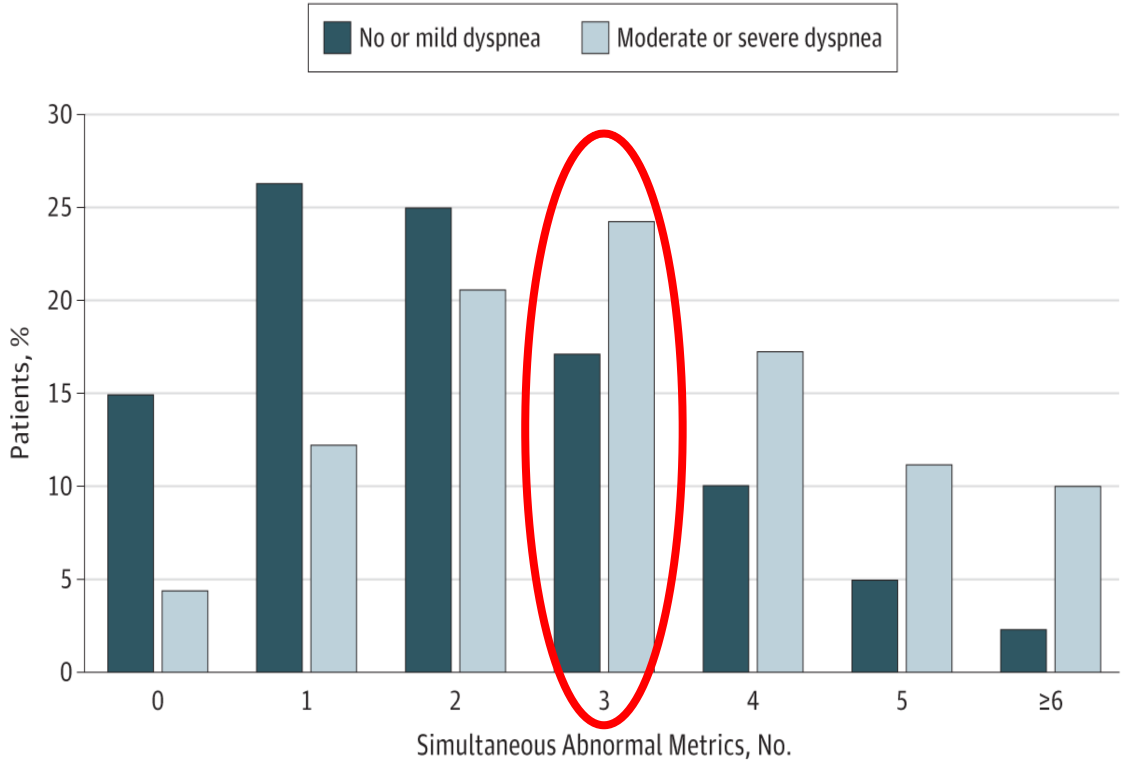
BOLD Study: ~27% in those ≥40 years old across 15 countries (n=9,484)
Related to older age, female sex, overweight/obesity, smoking history, reduced lung function, presence of cardiorespiratory disease, childhood infections/hospitalizations, lower SES

SCAPIS: ~10%
Main contributing conditions: 1) respiratory disease (57%), 2) anxiety/depression (52%), 3) obesity (43%), heart disease (35%)

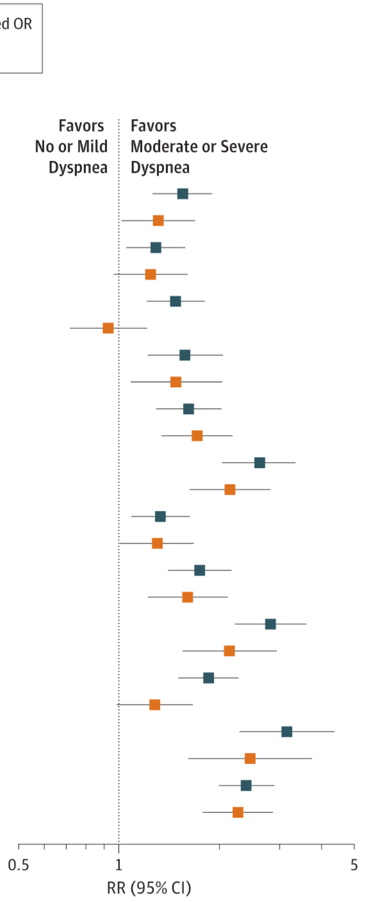


Grønseth R, Eur Respir J, 2014
Sandberg J, BMJ Open Respir Res, 2020

Association of Undifferentiated Dyspnea in Late Life With Cardiovascular and Noncardiovascular Dysfunction - A Cross-sectional Analysis From the ARIC Study



Dysfunction	Dyspnea, No. (%) No or Mild (n = 3768)	Dyspnea, No. (%) Moderate or Severe (n = 574)	Age, Race/Ethnicity, and Sex Adjusted OR (95% CI)	Fully Adjusted OR (95% CI)	Population-Attributable Risk, % (95% CI)
LV hypertrophy	825 (22.0)	172 (30.3)	1.53 (1.25-1.87)	1.30 (1.01-1.67)	5.8 (2.5-11.1)
LV systolic dysfunction	953 (25.3)	175 (30.5)	1.28 (1.05-1.56)	1.23 (0.96-1.58)	NA
LV diastolic dysfunction	894 (23.7)	193 (33.6)	1.46 (1.20-1.78)	0.93 (0.72-1.21)	NA
Pulmonary hypertension	355 (9.4)	92 (16.0)	1.56 (1.21-2.01)	1.47 (1.08-2.00)	4.0 (0.3-7.6)
Obstructive ventilatory pattern	891 (29.9)	162 (37.9)	1.59 (1.28-1.99)	1.69 (1.33-2.14)	13.0 (6.8-18.8)
Restrictive ventilatory pattern	394 (13.2)	113 (26.5)	2.56 (1.99-3.27)	2.11 (1.61-2.76)	10.7 (6.3-14.9)
Renal dysfunction	875 (23.3)	181 (31.8)	1.32 (1.08-1.61)	1.29 (1.01-1.65)[a]	NA
Anemia	570 (15.1)	156 (27.2)	1.72 (1.39-2.12)	1.59 (1.21-2.07)	8.8 (4.9-12.4)
Lower extremity weakness	296 (7.9)	141 (24.6)	2.77 (2.18-3.51)	2.10 (1.53-2.88)	8.5 (4.6-12.3)
Upper extremity weakness	843 (22.6)	198 (35.3)	1.82 (1.49-2.23)	1.27 (0.98-1.64)	NA
Depression symptoms	133 (3.5)	64 (11.2)	3.01 (2.24-4.25)	2.41 (1.59-3.66)	4.8 (2.3-7.3)
Obesity	1056 (28.1)	259 (45.3)	2.35 (1.95-2.83)	2.22 (1.75-2.81)	22.6 (16.0-28.7)



Ramalho SHR, JAMA Netw Open, 2019

Cardiopulmonary Exercise Testing

“Cardiopulmonary exercise testing (CPET) provides a global assessment of the integrative exercise responses involving the pulmonary, cardiovascular, hematopoietic, neuropsychological, and skeletal muscle systems, which are not adequately reflected through the measurement of individual organ system function...........The use of CPET in patient management is increasing with the understanding that resting pulmonary and cardiac function testing cannot reliably predict exercise performance and functional capacity and that, furthermore, overall health status correlates better with exercise tolerance rather than with resting measurements.”

“is based on the principle that system failure typically occurs while the system (e.g., muscle–energetic, cardiovascular or pulmonary) is under stress”

“To assess exertional breathlessness you must exert the breathless”

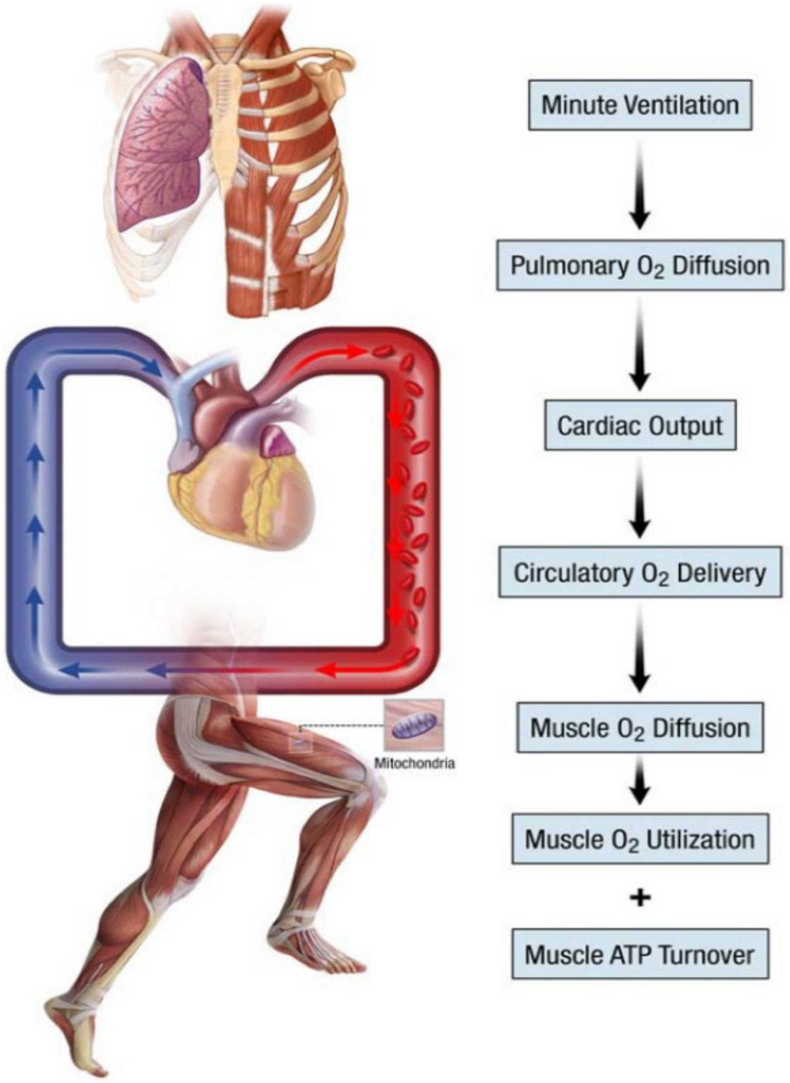
ATS/ACCP Statement on Cardiopulmonary Exercise Testing, Am J Respir Crit Care Med, 2001
Palange P, Eur Respir J, 2007
La Gerche A, Eur J Heart Fail, 2013

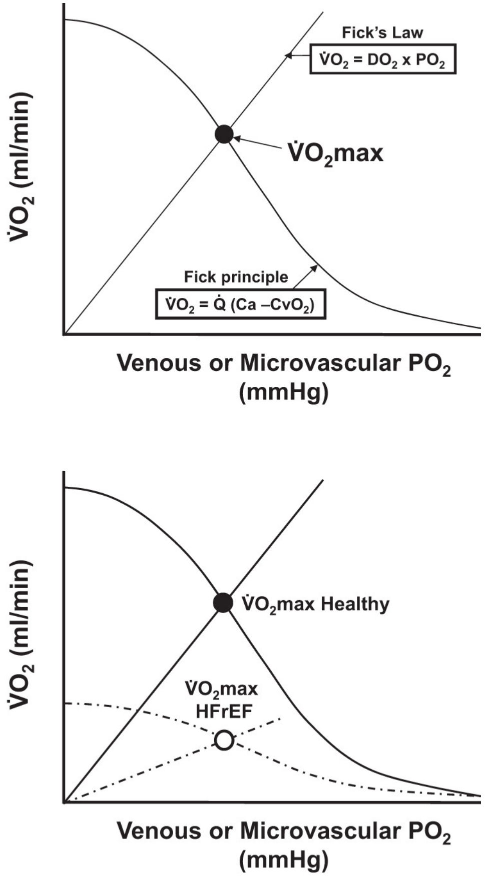
Indications for Cardiopulmonary Exercise Testing

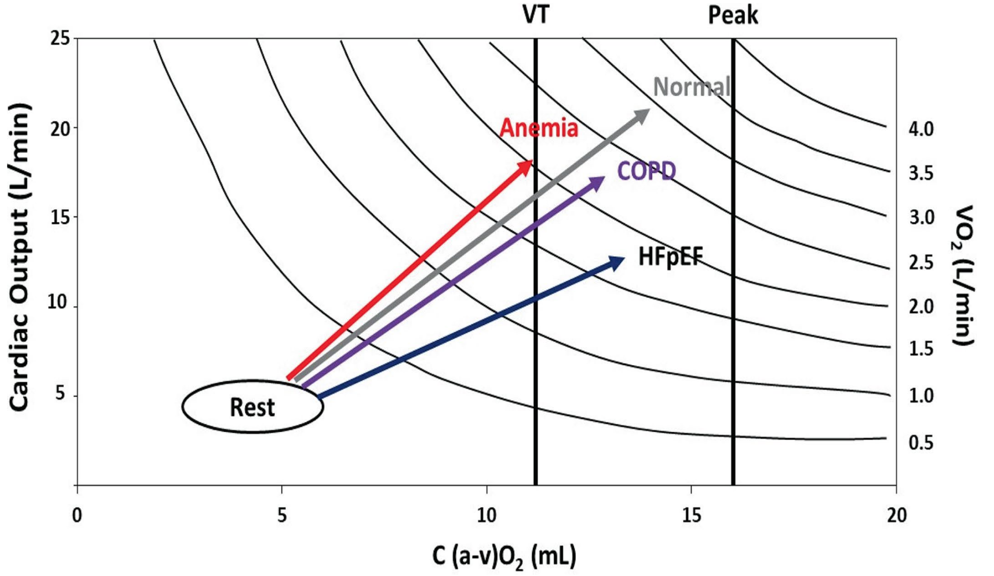
- Evaluation of exercise tolerance
- Evaluation of undiagnosed exercise intolerance
  - Unexplained dyspnea - initial testing nondiagnostic/ disproportionate to resting tests
  - Contribution of coexistent cardiac and pulmonary disease
- Evaluation of patients with cardiovascular disease
  - Risk stratification and prognosis in HF patients
  - Selection for advanced HF therapies
- Evaluation of patients with respiratory disease
- Preoperative evaluation
- Evaluation of impairment/disability
- Exercise prescription for cardiopulmonary rehabilitation

ATS/ACCP Statement on Cardiopulmonary Exercise Testing, Am J Respir Crit Care Med, 2001

The Oxygen Cascade







Dominelli PB, Mayo Clinic Proc, 2021
Poole DC, J Appl Physiol, 2018
Guazzi M, Eur J Heart Fail, 2022

Evaluation of Dyspnea with CPET

- Used to uncover the cause(s) of exertional dyspnea/exercise intolerance in those with cardiorespiratory disease or abnormal S/S
- Resting physiologic tests (i.e., PFTs, echo) may poorly predict exertional dyspnea
- Exercise intolerance (dyspnea/fatigue) is often multifactorial
- "Response modifiers" such as polypharmacy, obesity, sedentarism, anxiety, and anemia must be considered
- Versus giving a diagnosis it serves to describe patterns of abnormality that can be used to shorten the differential diagnosis and guide further evaluations and/or treatments

Table 2
Integrated approach to cardiopulmonary exercise testing (CPET)

Interpretation Step	Key Variables to Assess
1. General test overview	• Review indication for CPET • Assess test quality • Assess maximal test criteria • Determine degree of exercise limitation and reason for exercise cessation
2. Baseline resting data	• Demographic data (age, sex, BMI) • Resting vital signs (BP, HR, SpO_2, breathing frequency) • Resting spirometry • Resting 12-lead ECG
3. Perceptual response	• Assessment of dyspnea and leg fatigue using standardized scale (eg, Borg scale) • Dyspnea/WR; dyspnea/$\dot{V}O_2$; dyspnea/$\dot{V}_E$
4. Ventilatory control	• $\dot{V}_E$ • $\dot{V}_E$-$\dot{V}CO_2$ (nadir, slope and intercept) • SpO_2 • $P_{ET}CO_2$ • Pa_{CO_2} • AT • RER
5. Dynamic respiratory mechanics	• Exercise flow-volume loops relative to maximal resting flow-volume loops • IC • IRV • VT • Fb
6. Cardio vascular	• $\dot{V}O_2$/WR • HR • O_2 pulse
7. Integration and interpre tation	• Review of pattern of physiologic limitation considering the degree of exercise impairment, perceptual, ventilatory, respiratory mechanical and cardiovascular responses

O'Donnell, Clin Chest Med, 2019
Palange P, ERS Monograph, 2018

Methodology of CPET

Pre-test Considerations

- Test Indication
- Smoking Status
- PA levels
- Anthropometrics
- Hemoglobin levels
- Medications
- Pre-exercise PFTs
- PPM/ICD parameters

Standard Exercise Test Variables

- Treadmill or bicycle ergometer
- 8-12 minutes of incremental exercise
- Symptom-limited effort
- ECG
- HR response
- Blood pressure
- Pulse oximetry
- Symptom Responses
    - perceived exertion (RPE)
    - dyspnea
    - chest pain

Ventilatory Gas-Analysis

VO_2

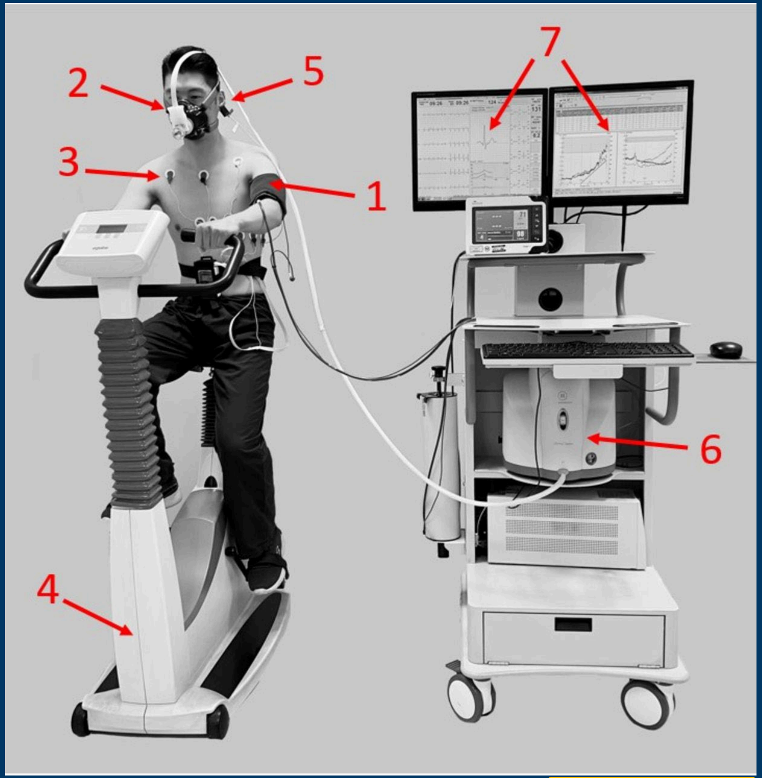
VCO_2

Minute ventilation

Respiratory rate

Tidal volume

End-tidal O_2 & CO_2



Pritchard A, BMJ Open Resp Res 2021

CPET Parameters

- Quantification of Exercise Intolerance/ Functional Capacity Assessment
- Cardiovascular Limitation
- Pulmonary Mechanical Limitation
- Gas-Exchange Limitation

Interpretation

Sun XG, Eur J Appl Physiol, 2011
Guazzi M, Eur J Heart Fail, 2022

Quantification of Exercise Intolerance/ Functional Capacity Assessment

- Respiratory Exchange Ratio (RER)
- Peak Oxygen Consumption/Uptake (VO_2)
- VO_2 @ VAT (Ventilatory Threshold-1)
  - % of predicted peak VO_2
- Oxygen Uptake Efficiency Slope (OUES)
  - Submaximal parameter that strongly correlates with peak VO_2 (R-value ~0.9)

Sun XG, Eur J Appl Physiol, 2011
Guazzi M, Eur J Heart Fail, 2022

Importance of Assessing Cardiorespiratory Fitness in Clinical Practice: A Case for Fitness as a Clinical Vital Sign: A Scientific Statement From the American Heart Association

Robert Ross, Steven N. Blair, Ross Arena, Timothy S. Church, Jean-Pierre Després, Barry A. Franklin, William L. Haskell, Leonard A. Kaminsky, Benjamin D. Levine, Carl J. Lavie, Jonathan Myers, Josef Niebauer, Robert Sallis, Susumu S. Sawada, Xuemei Sui, and Ulrik Wisløff
and On behalf of the American Heart Association Physical Activity Committee of the Council on Lifestyle and Cardiometabolic Health; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Council on Cardiovascular and Stroke Nursing; Council on Functional Genomics and Translational Biology; and Stroke Council

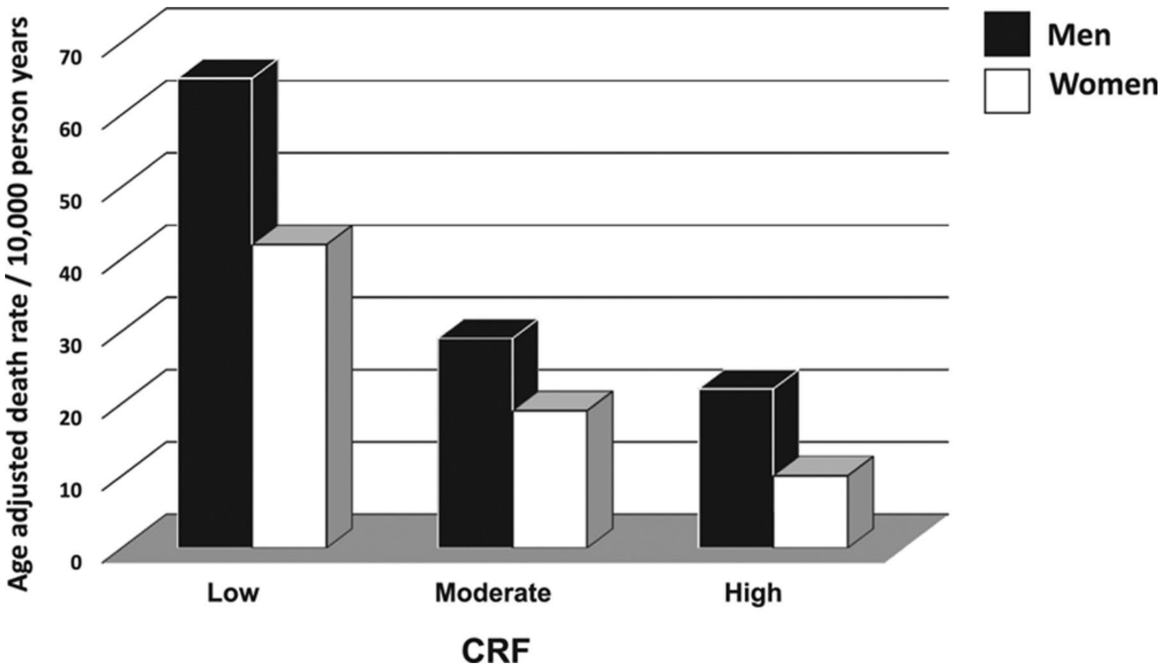


Figure. All-cause death rates across categories of cardio-respiratory fitness (CRF) in 3,120 women and 10,224 men.

Legend: Low=<5-METS; Moderate=5-8 METS; High=>8 METS

Blair et al., JAMA, 1989

Conclusions and Recommendations: CRF as a Predictor of Health Outcomes

- CRF is as strong a predictor of mortality as established risk factors such as cigarette smoking, hypertension, high cholesterol, and T2DM.
- A CRF level <5 METs in adults is associated with high risk for mortality; CRF levels >8 to 10 METs are associated with increased survival.
- More than half the reduction in all-cause mortality occurs between the least fit (eg, CRF <5 METs) group and the next least fit group (eg, CRF 5–7 METs).
- The influence of race on the relationship between CRF and health outcomes requires further investigation.
- Small increases in CRF (eg, 1–2 METs) are associated with considerably (10% to 30%) lower adverse cardiovascular event rates.
- Efforts to improve CRF should become a standard part of clinical encounters (eg, an accepted "vital sign").

Ross R, Circulation, 2016

Importance of directly measuring exercise capacity (VO_2) versus estimation

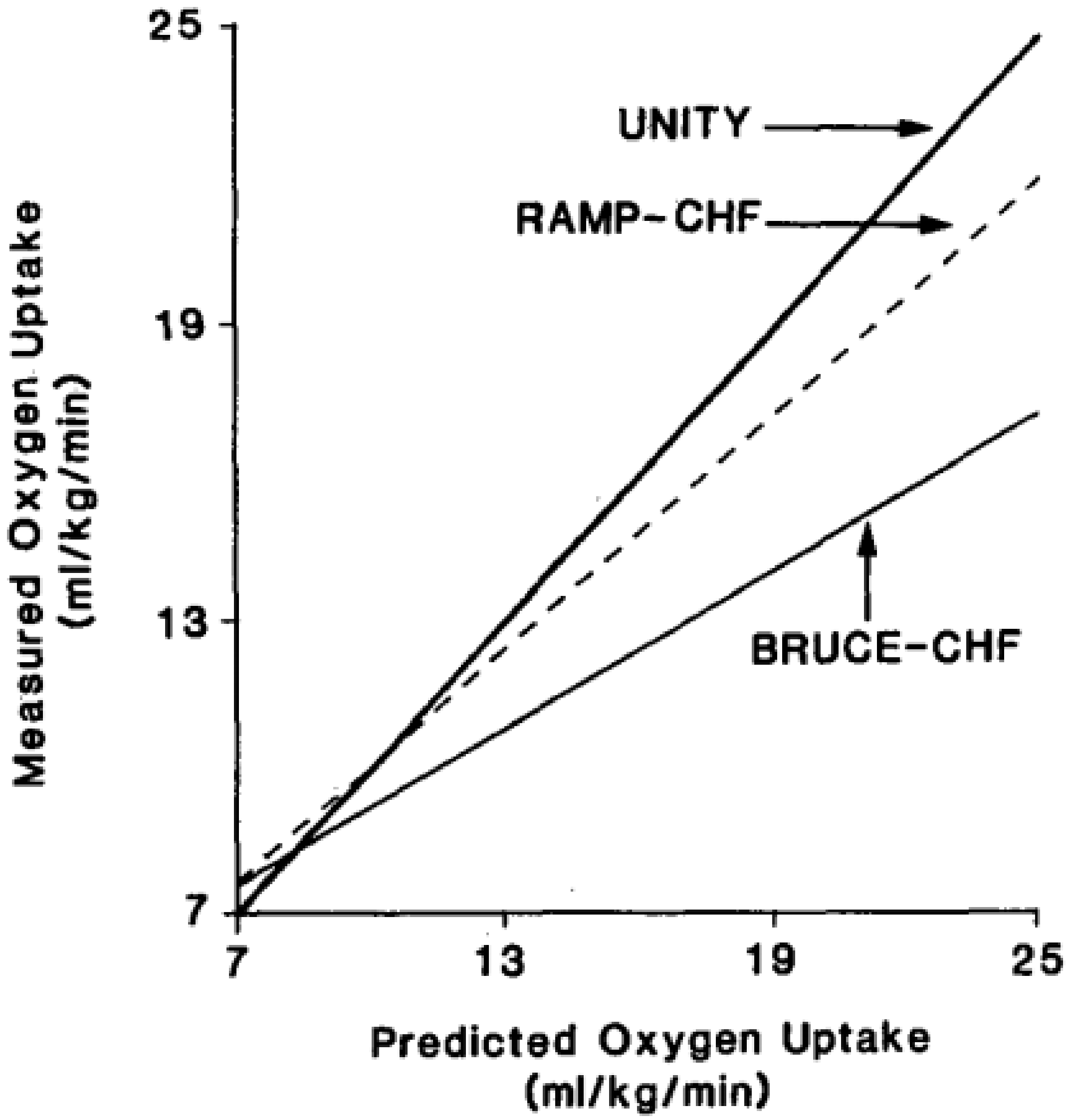


Table 4. Slopes in Oxygen Uptake Versus Work Rate for 40 Subjects Performing the Six Exercise Protocols

	Treadmills			Bicycles		
	Bruce	Balke	Ramp	25 W	50 W	Ramp
Slope	0.62	0.79	0.80	0.69	0.59	0.78
SEE	4.0	3.4	2.5	2.3	2.8	1.7

Each slope ≥0.78 was significantly different from each slope ≤0.69 ($p < 0.05$ except Balke vs. 25 W, $p = 0.07$). If the change in ventilatory oxygen uptake was equal to the change in work rate, the slope would be equal to 1.0. SEE = standard error of the estimate (ml oxygen/kg per min): 25 W = 25 W/stage; 50 W = 50 W/stage.

Table 5. Slopes in Oxygen Uptake Versus Work Rate for Each Patient Subgroup Performing Each of the Six Exercise Protocols

	CAD	Angina	CHF	Normal
Slope	0.51	0.53	0.53	0.71*
SEE, ml O_2/kg per min	2.6	3.1	2.8	4.2

*$p < 0.001$ versus other groups. CAD = coronary artery disease; CHF = chronic heart failure. If the change in ventilatory oxygen uptake was equal to the change in work rate, the slope would be equal to 1.0.

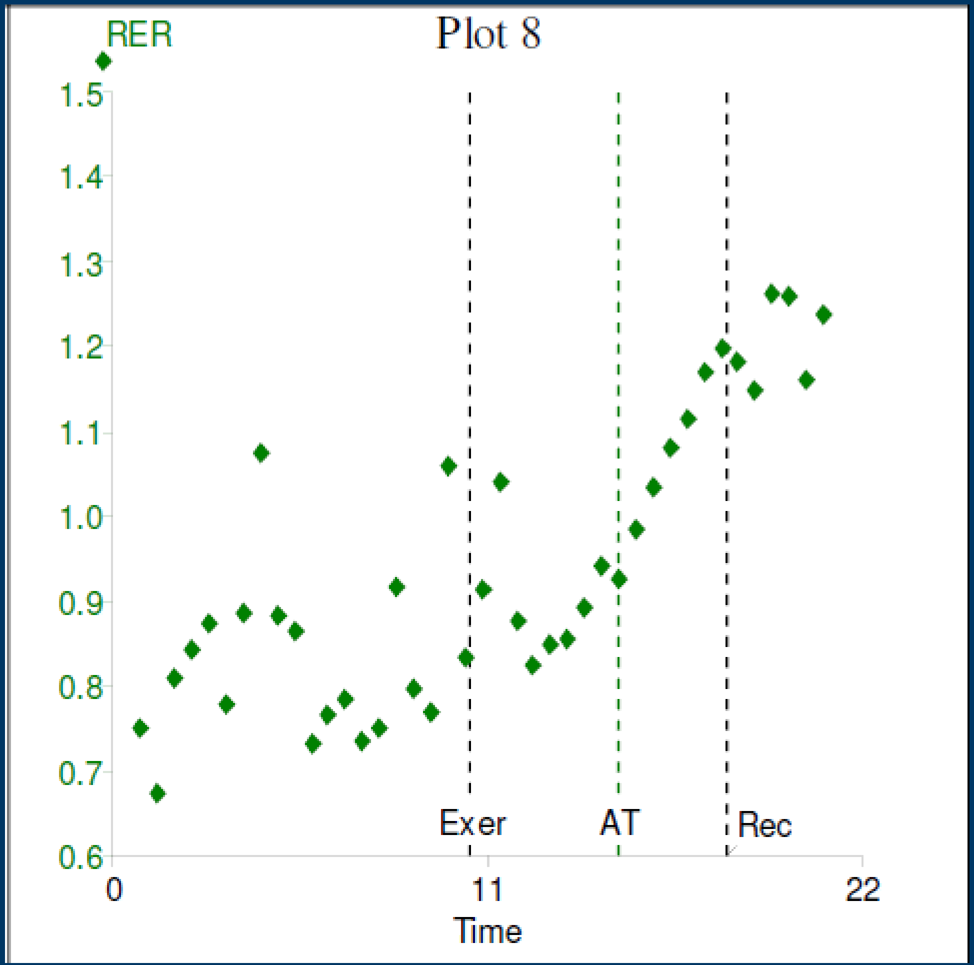
Myers J, J Am Coll Cardiol, 1991

Respiratory Exchange Ratio (RER)

Ratio of VCO_2/VO_2

Most accurate and reliable gauge of subject effort

- >1.10 indicates excellent subject effort
- >1.05 used as indication for advanced HF therapy consideration
- >1.00 minimally-acceptable effort
- <1.00 generally reflects submaximal cardiovascular effort in absence of electrocardiographic or hemodynamic abnormalities or pulmonary limitation to exercise



Balady GJ, Circulation, 2010

Peak Oxygen Consumption/Uptake

Gold-standard assessment of cardiorespiratory fitness

high test-retest reliability (ICC's > 0.9)

Absolute values (L/min or mL/min)

- dependent upon age, sex, anthropometrics (HT/WT)

Relative values ($mL \cdot kg^{-1} \cdot min^{-1}$)

%-predicted peak VO_2

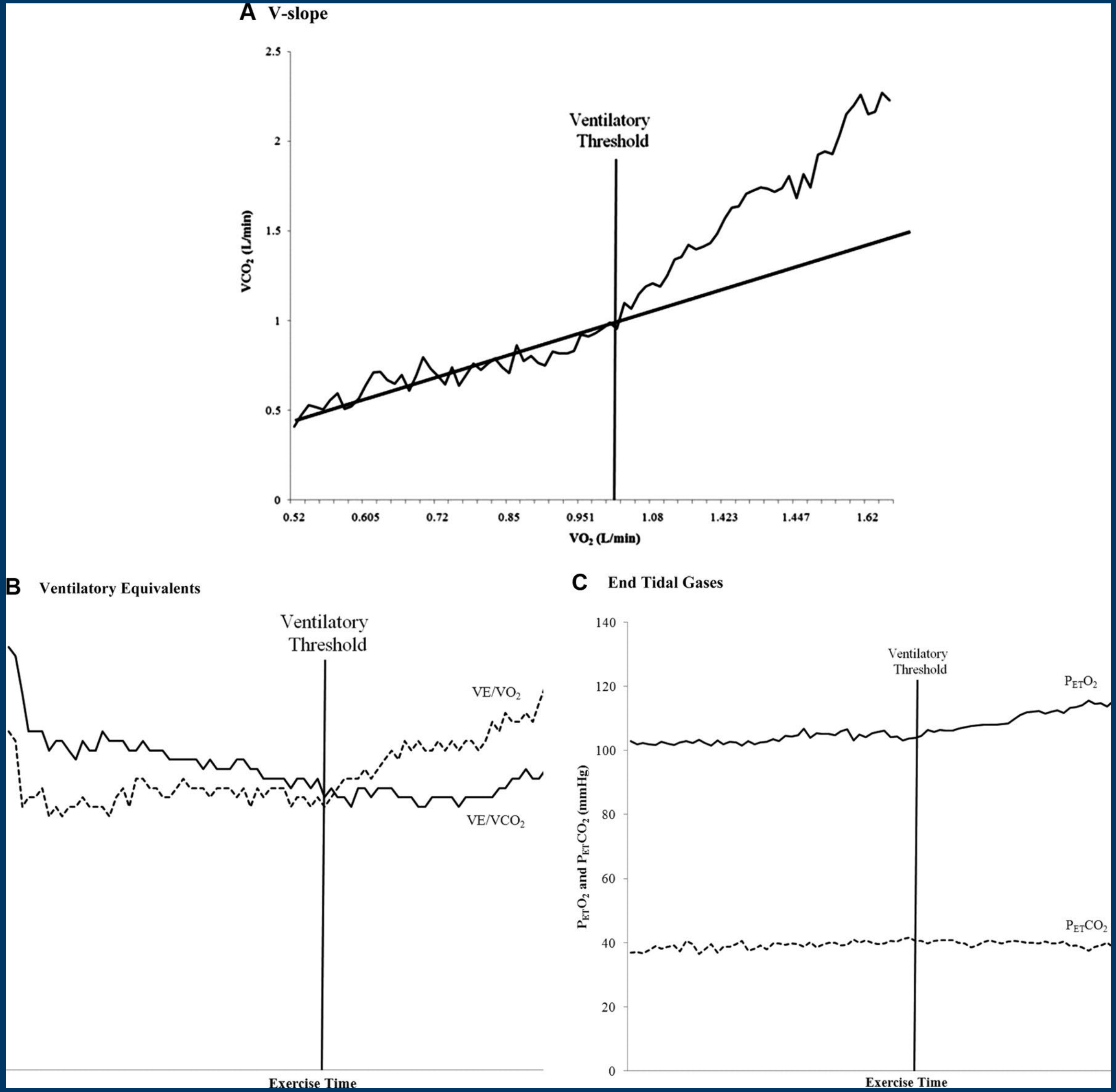
- <85% of predicted = Abnormal
- Wasserman/Hansen prediction equations most often used
- Significant discrepancies b/t %-predicted absolute and relative values may indicate impact of obesity

Weber-Janicki Functional Classification of Cardiac Reserve		
Classification	**Peak VO_2 ($mL \cdot kg^{-1} \cdot min^{-1}$)**	**Max Cardiac Index ($mL/min/m^2$)**
A. Normal	**>20**	**>8**
B. Mild to moderate impairment	**16-20**	**6-8**
C. Moderate to severe impairment	**10-15.9**	**4-6**
D. Severe impairment	**<10**	**2-4**

Guazzi M, Eur J Heart Fail, 2022
Laveneziana P, Eur Respir Rev, 2021
Bernhardt V, Eur Respir Rev, 2016
Weber K & Janicki JS, Am J Cardiol, 1985

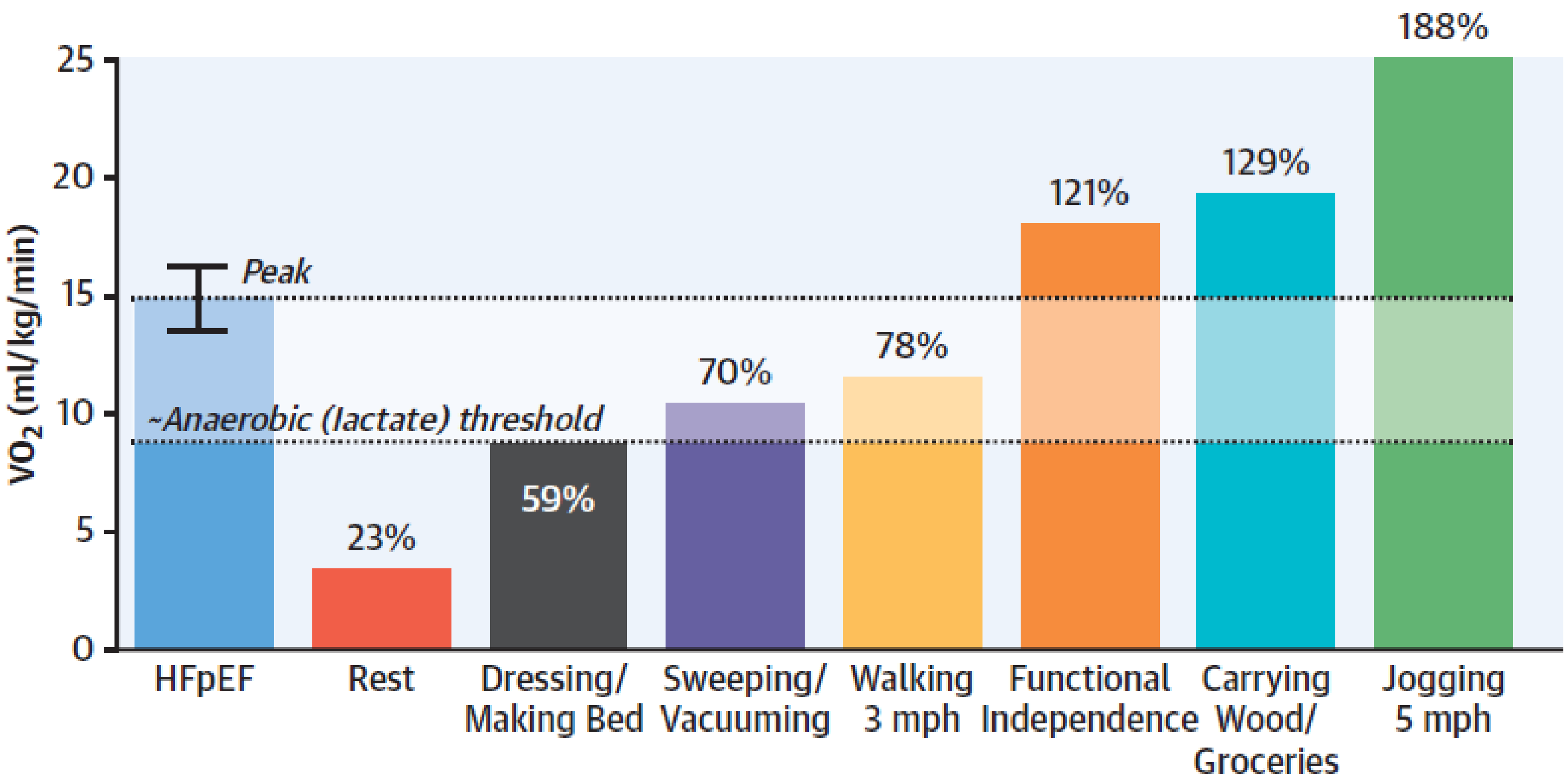
Ventilatory Anaerobic Threshold (VAT, AT, VT)

- Submaximal index of CRF compatible with sustainable ADL tolerance
- VO_2 at which minute ventilation (VE) begins to increase exponentially relative to the increase in VO_2
- a reflection of lactate threshold
- generally, occurs @ >40 to 65% of peak VO_2



Balady GJ, Circulation, 2010

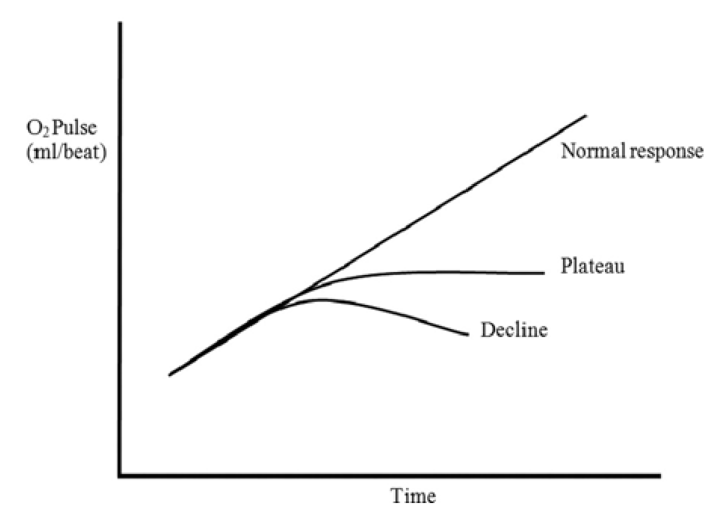
Peak VO_2 Required for Activities of Daily Living Relative to Average Peak VO_2 Observed in HFpEF

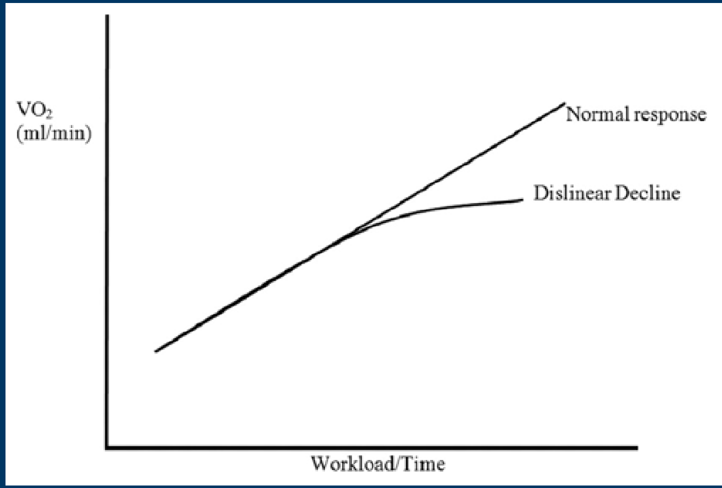


Nayor, M. et al. J Am Coll Cardiol HF. 2020;■(■):■-■.

Cardiovascular Limitation – noninvasive CPET

- Heart rate response
  - ≥85-90% predicted max HR
  - Metabolic chronotropic index (≤0.80 or <0.62 on beta-blocker)
- Oxygen pulse (mL/beat): ≤80% predicted
  - Oxygen pulse trajectory (flattening or decline in slope)
  - Noninvasive surrogate for stroke volume
- VO2/Work rate relationship (<8.4 mL/min/Watt)
  - VO2/WR trajectory (flattening or decline in slope)
- Electrocardiogram (ST segment changes, arrhythmias, pacemaker loss/malfunctioning)
- Blood pressure (hypotensive, hypertensive response)
- Presence of angina pectoris

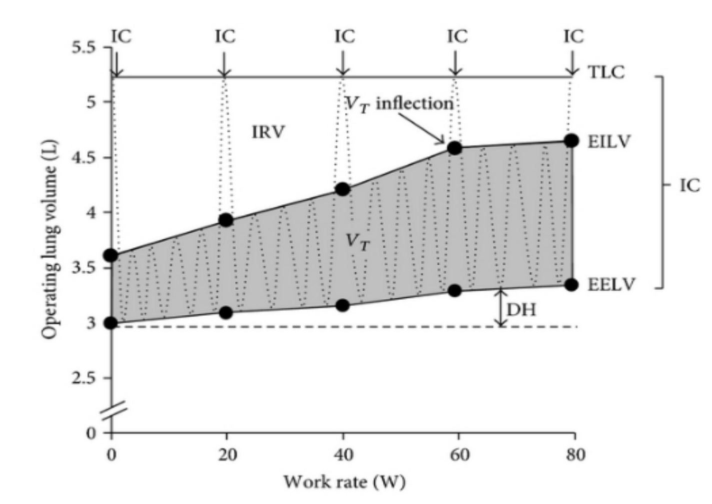


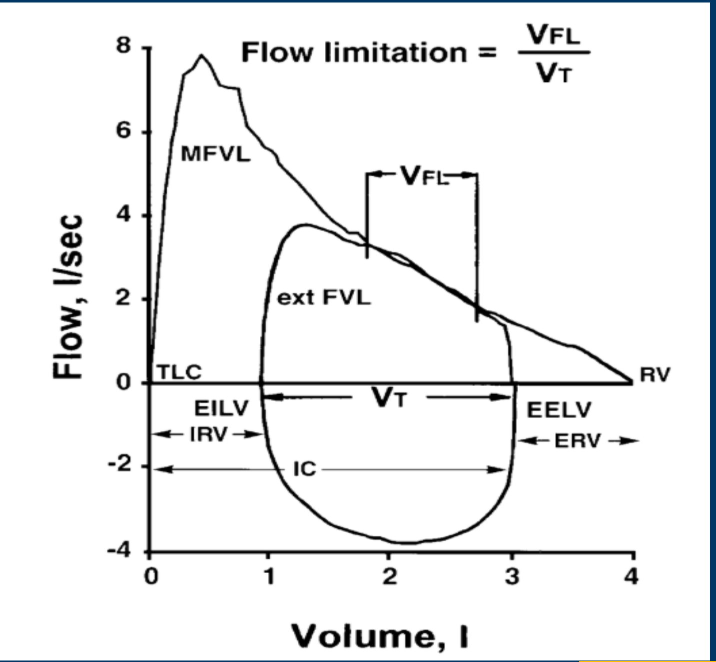


Balady GJ, Circulation, 2010
Guazzi M, Eur J Heart Fail, 2022
ATS/ACCP Statement on Cardiopulmonary Exercise Testing, Am J Respir Crit Care Med, 2001

Pulmonary Mechanical Limitation – nonivasive CPET

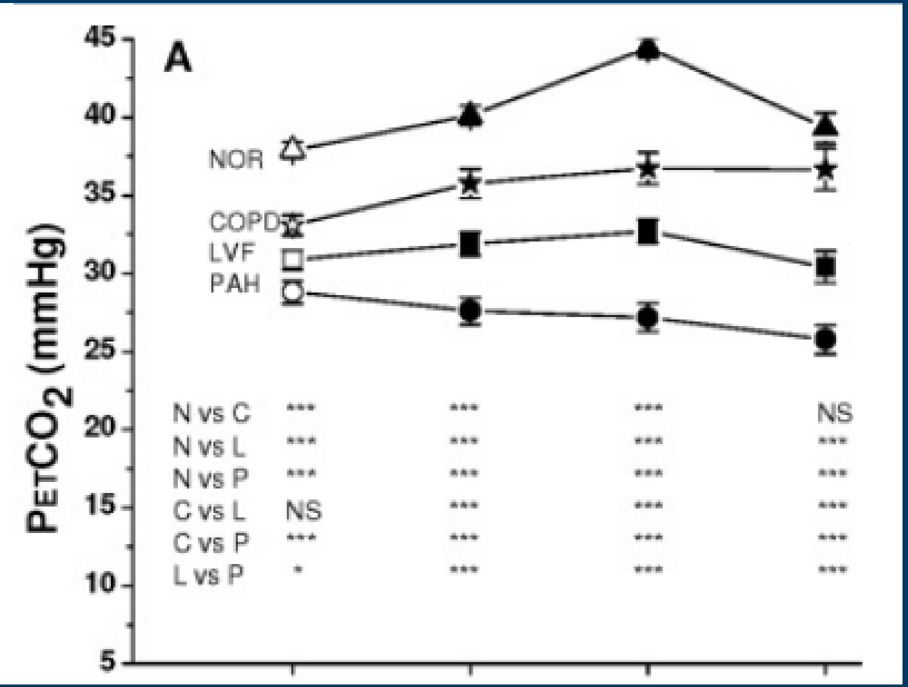
- Pre-exercise spirometry (FVC, FEV-1, IC, MVV)
- Minute Ventilation (VE) to Maximal Voluntary Ventilation ratio (MVV)
  - VE/MVV: >0.80-0.85
  - Breathing reserve (%): <15-20%
- Tidal volume (V_T) to Inspiratory Capacity (IC) ratio
  - V_T/IC >70% (80% upper 95% confidence limits)
- Respiratory rate
  - >50-55 breaths per minute
- Exercise tidal flow-volume loops
  - EFL >25% overlap at peak
  - Leftward shift of ExeFVL during exercise
- Serial exercise IC measurements
  - >140 mL decrease





Gas-exchange Limitation – noninvasive CPET

- SpO_2
  - <95% at rest and/or ≥5% decrease with exercise
- VE/VCO_2 slope
  - Relationship of ventilation (VE) and carbon dioxide production (VCO_2)
- End-tidal CO_2
  - Normal: 36-42 mmHg, increases 3-8 mmHg with exercise, decreases at peak exercise d/t respiratory compensation



REST VAT PEAK

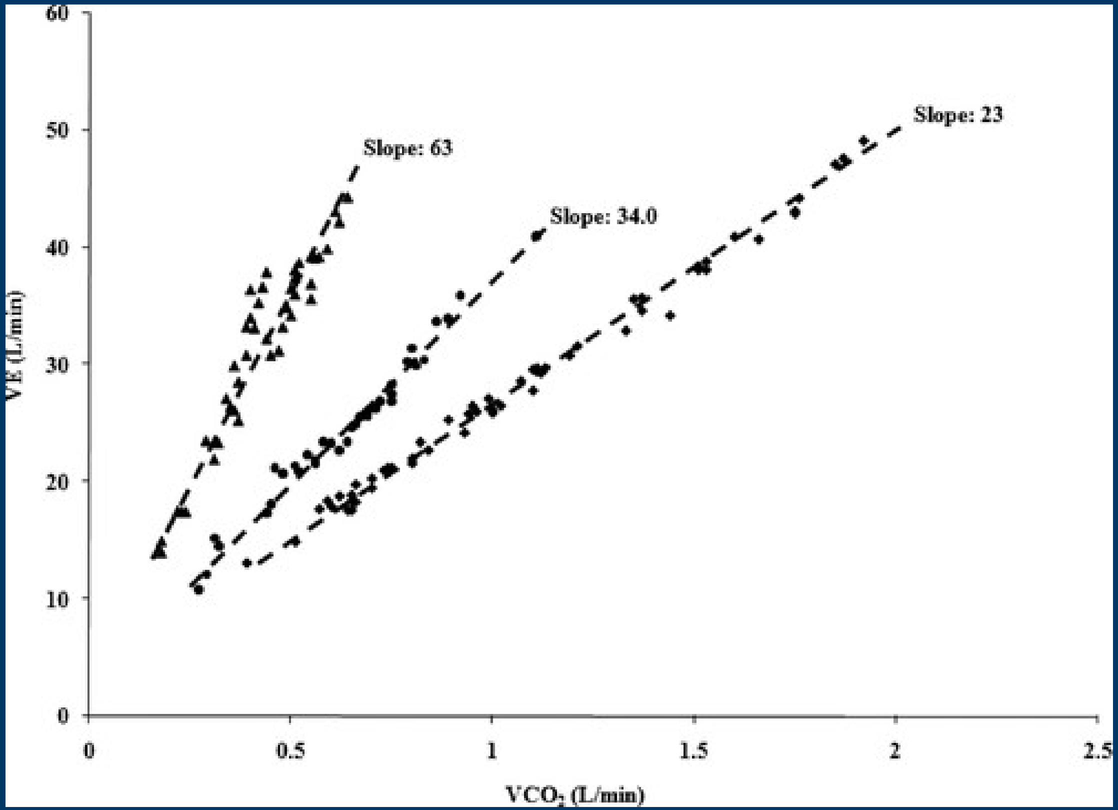
Guazzi M, Eur J Heart Fail, 2022
Guazzi M, Circulation, 2012
Hansen J, CHEST, 2007
Taivassalo T, Brain, 2003

Ventilatory Efficiency (VE/VCO_2 slope)

- Reflects ventilation-perfusion matching, chemoreceptor and ergoreceptor sensitivity
- Globally indicates severity of cardiopulmonary disease

Expressions:

- Most often expressed as slope throughout the entire exercise period
  - slope up to respiratory compensation
- VE/VCO_2 @ VAT and VE/VCO_2 nadir (very similar)
- VE/VCO_2 Intercept
  - may discriminate HF from COPD

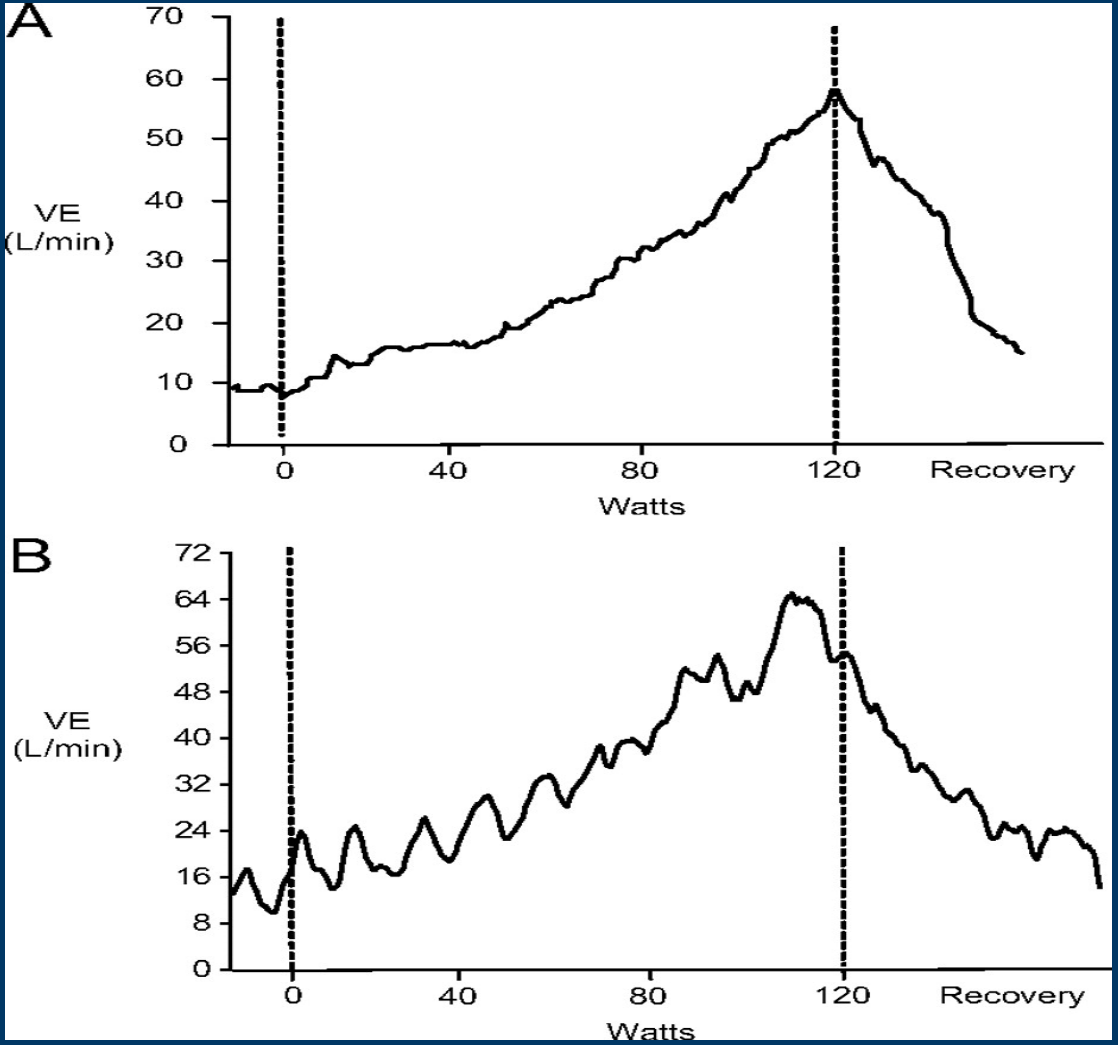


HF Ventilatory Classification System	
Class	VE/VCO_2 Slope
I	≤29.9
II	30.0 – 35.9
III	36.0 – 44.9
IV	≥45.0

Balady GJ, Circulation, 2010; Arena R, Circulation, 2007
Guazzi M, Eur J Heart Fail, 2022

Exercise Oscillatory Ventilation (EOV) or Exercise Periodic Breathing

- Cyclic fluctuations in ventilation at rest that persist into exercise
- complex phenomenon that appears to be the result of the deregulation of different mechanisms involved in the mechanical and neural feedback control of the cardiopulmonary system
- Strong predictor of sudden cardiac death



Balady GJ et al., Circulation, 2010; 122:191-225

Symptom Perception

- Reason for test termination
- Secondary symptoms (i.e., paresthesia, lightheaded/dizziness, claudication)
- Rating of perceived exertion (RPE)
- Rating of perceived dyspnea

Rating of Perceived Exertion	
6	Nothing at all
7	Very, Very Light
8	
9	Very Light
10	
11	Fairly Light
12	
13	Somewhat Hard
14	
15	Hard (Heavy)
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

Rating of perceived dyspnea	
0	Nothing at all
0.5	Very, very slight
1	Very slight
2	Slight
3	Moderate
4	Somewhat severe
5	Severe
6	
7	Very Severe
8	
9	Very, very severe
10	Maximal

Arena R, Expert Rev Cardiovasc Ther, 2020
Guazzi M, Circulation, 2012

Composite CPX Score

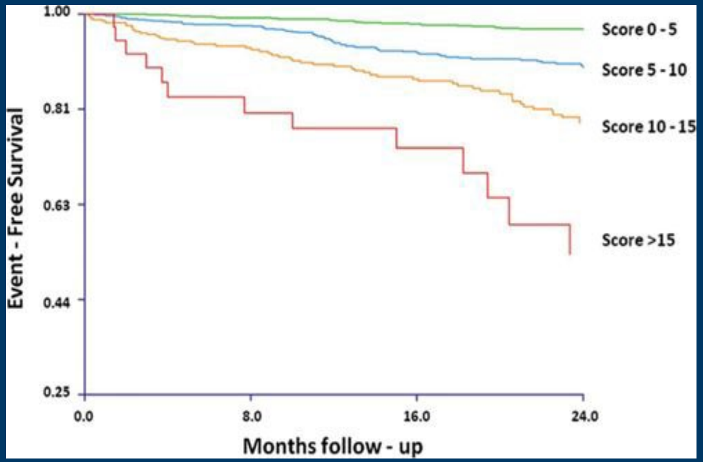
CPX Responses	Weighted Scores
Peak VO_2 ≤ 14 ($mL \cdot kg^{-1} \cdot min^{-1}$)	2
HRR ≤ 6 bpm	5
VE/VCO_2 slope ≥ 34	7
OUES ≤ 1.4	3
Resting $PetCO_2$ < 33mmHg	3

Summed score >15 associated with annual mortality rate of 12.2% = High-risk

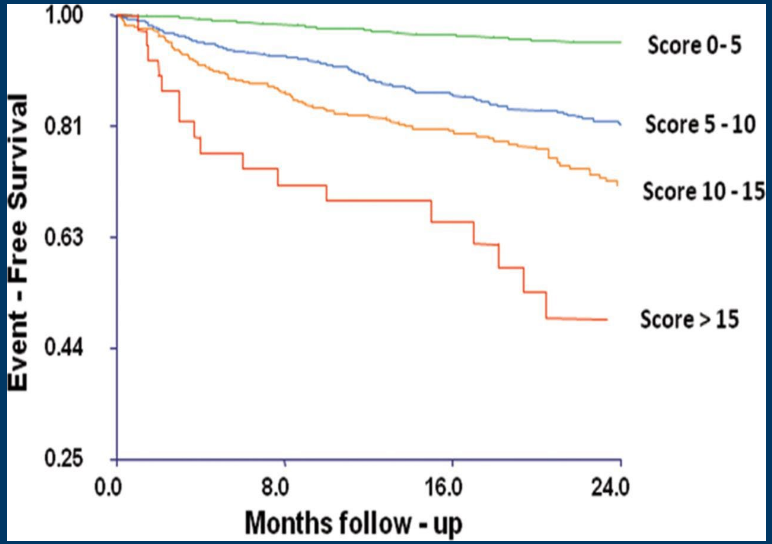
Summed score <5 associated with an annual mortality of 1.2% = Low-risk

Myers J et al., Circ. Heart Fail., 2013; 6:211-218

Kaplan–Meier curves illustrating cumulative survival for increasing CPX scores.



Kaplan–Meier curves illustrating event-free survival for the composite outcome by increasing CPX scores.



Usual cardiopulmonary exercise response patterns

Measurement	Heart Failure	COPD	ILD	Pulmonary Vascular Disease	Obesity	Deconditioned
$\dot{V}O_2$max or $\dot{V}O_2$peak	Decreased	Decreased	Decreased	Decreased	Decreased for actual, normal for ideal weight	Decreased
Anaerobic threshold	Decreased	Normal/decreased/ indeterminate	Normal or decreased	Decreased	Normal	Normal or decreased
Peak HR	Variable, usually normal in mild	Decreased, normal in mild	Decreased	Normal/ slightly decreased	Normal/ slightly decreased	Normal/ slightly decreased
O_2 pulse	Decreased	Normal or decreased	Normal or decreased	Decreased	Normal	Decreased
(VE/MVV) × 100	Normal or decreased	Increased	Normal or increased	Normal	Normal or increased	Normal
VE/VCO_2 (at AT)	Increased	Increased	Increased	Increased	Normal	Normal

Abbreviations: AT=anaerobic threshold; VCO_2=carbon dioxide output; VE=minute ventilation; VO_2=oxygen consumption; COPD=chronic obstructive pulmonary disease; ILD=interstitial lung disease; HR=heart rate; MVV=maximal voluntary ventilation

Modified version* of “Table 18. Usual cardiopulmonary exercise response patterns” from *ATS/ACCP Statement on Cardiopulmonary Exercise Testing*, Am J Respir Crit Care Med, 2001. *blood gas parameters removed.

ATS/ACCP Statement on Cardiopulmonary Exercise Testing – Table 18. Usual cardiopulmonary exercise response patterns

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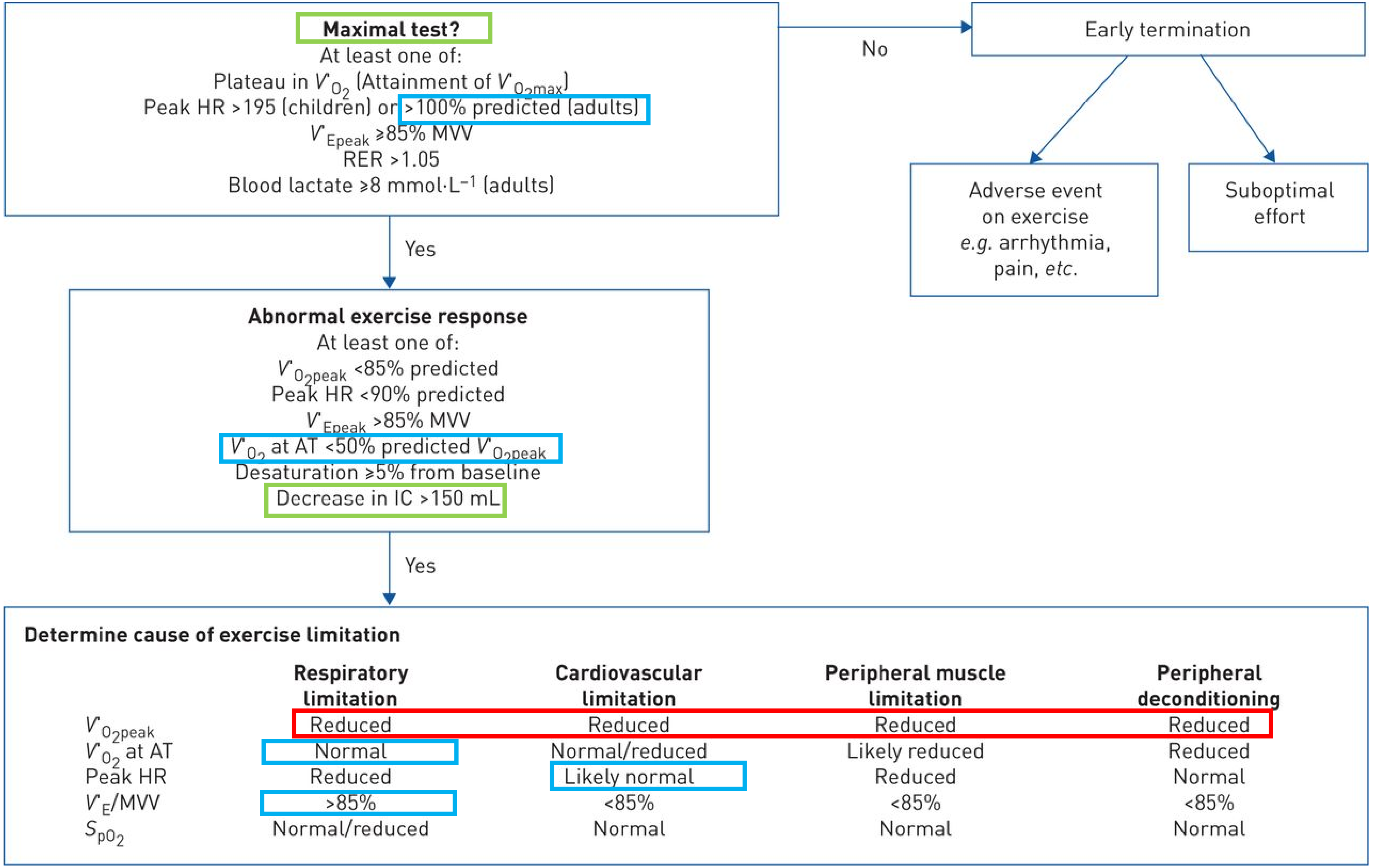
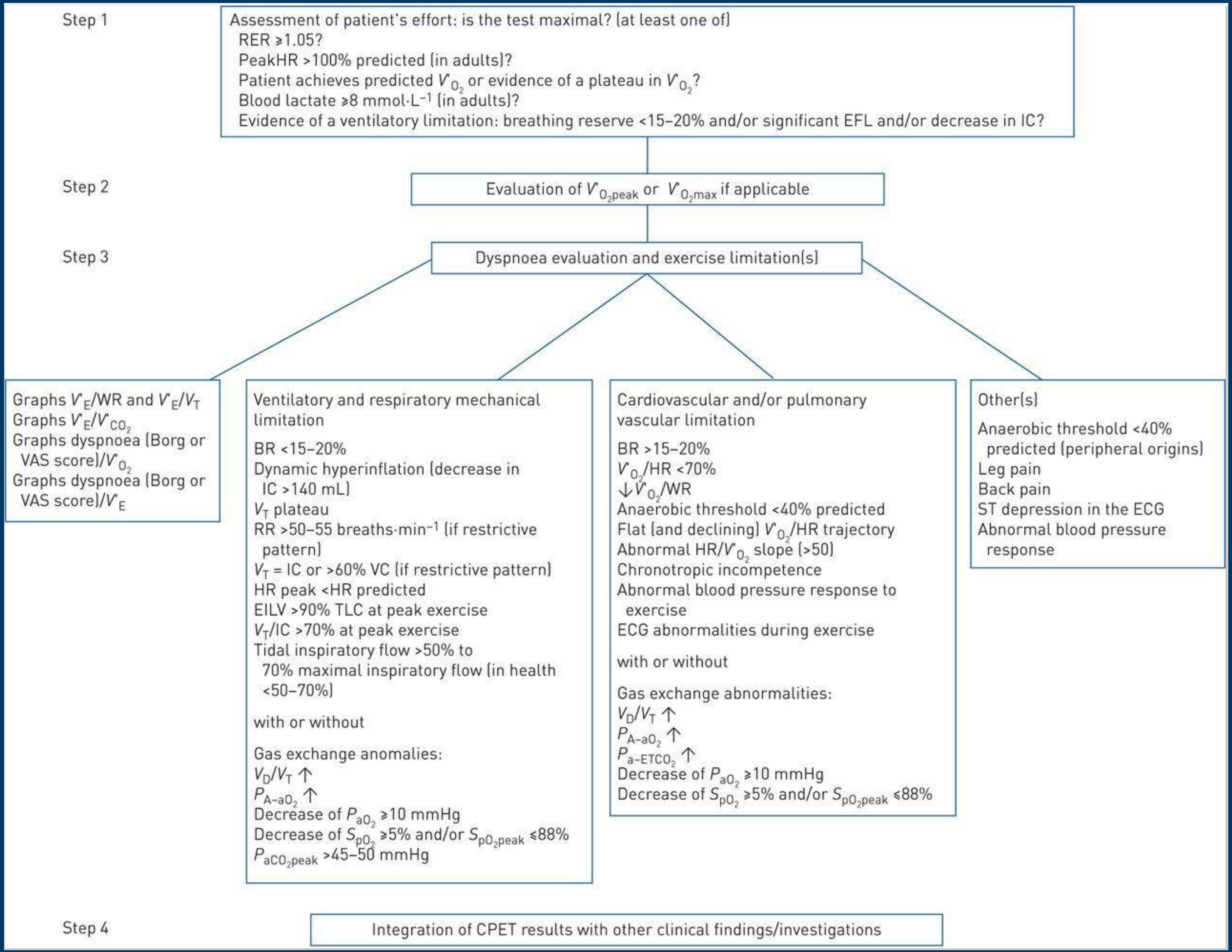
ERS statement on standardisation of cardiopulmonary exercise testing in chronic lung diseases



Radke T, European Respiratory Review, 2019



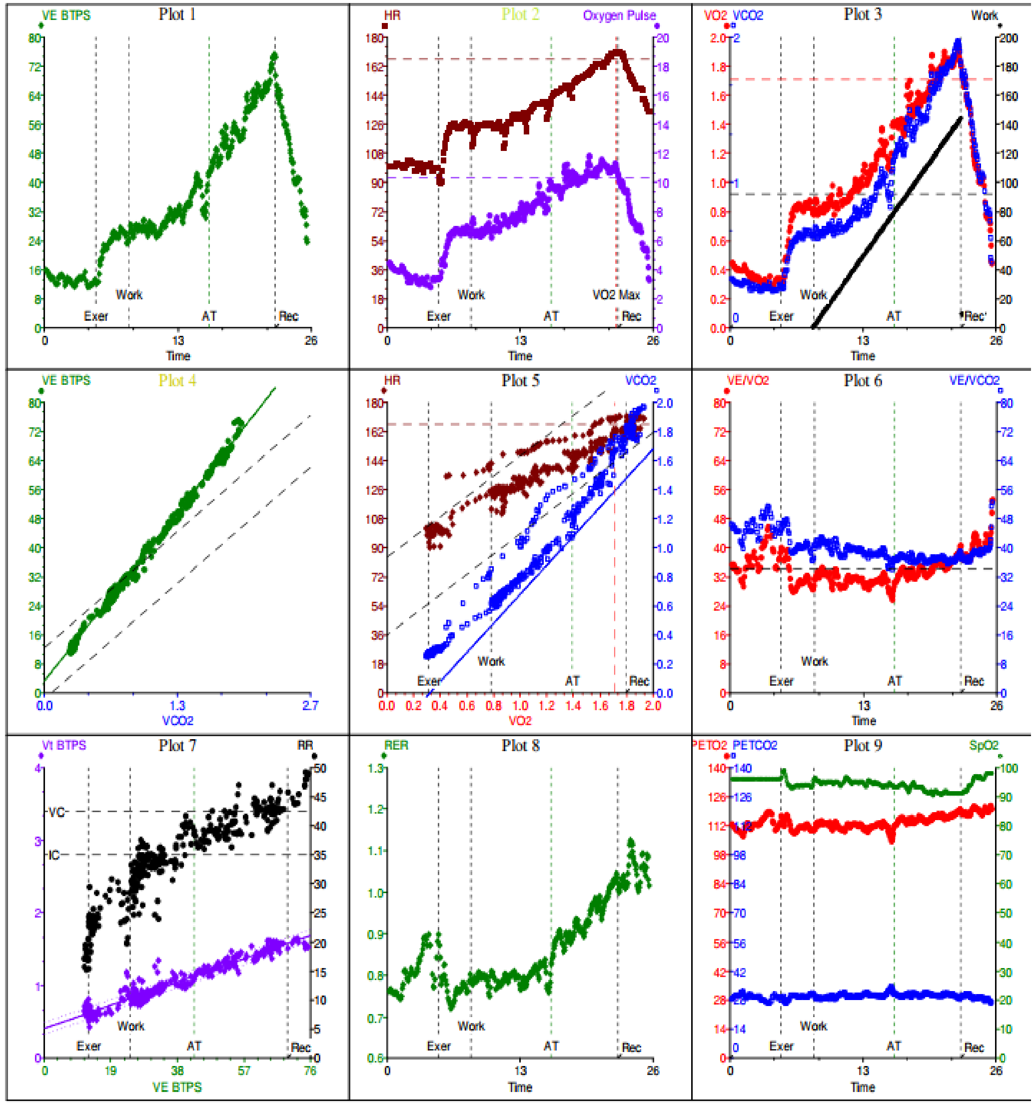
Laveneziana P, Eur Respir Rev, 2021

Case Study 1 - CPET Results

53yoF referred for CPET due to “dyspnea out of proportion to PFTs, exertional dyspnea” by outside pulmonologist

Bike-ergometer CPET with serial ExeFVL and IC maneuvers

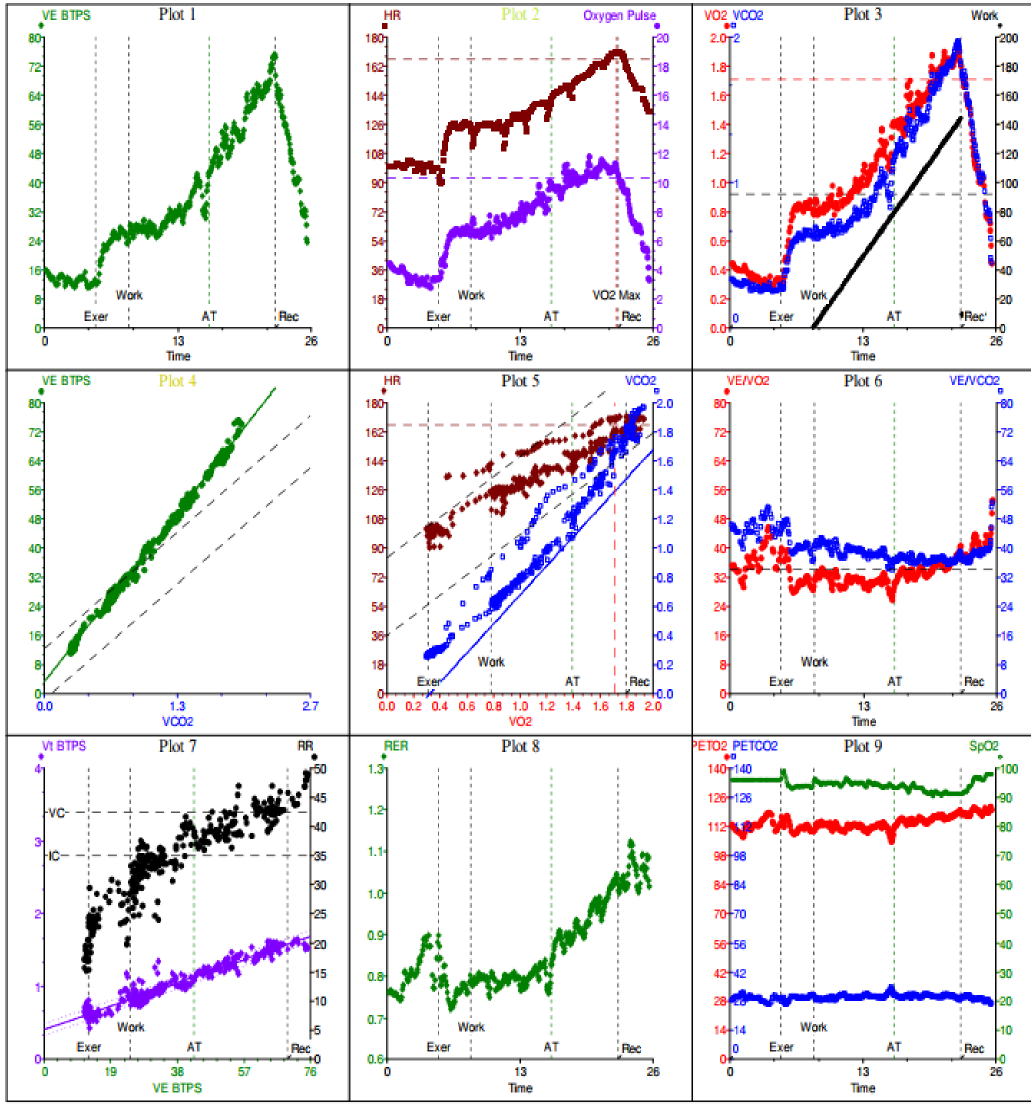
- Pre-Exe Spirometry:
  - FVC= 96%, FEV1= 92%, FEV1/FVC= 0.76
- Exercise Test Results:
  - Functional Capacity
    - Peak Watts = 142 (154%), VO2/WR slope= 8.5 mL/min/Watt
    - Peak VO2 = 1879 mL/min (110%);
    - relative VO2 = 17.3 mL/kg/min (76%)
    - Peak RER = 1.03
    - VAT= 74%
  - Cardiovascular Response
    - HR = 96 to 170 bpm (103%)
    - BP= 132/72 to 210/80 mmHg
    - Oxygen Pulse = 11.0 mL/beat (107%) – NL trajectory
    - Exercise ECG: NSR without ST-T wave changes or arrhythmias.
  - Ventilatory Response
    - Breathing reserve = 28%
    - V_T/IC = 57%
  - Gas-Exchange Response
    - SpO2 = 96% to 91%RA
    - VE/VCO2 slope = 34.6
  - Reason for Termination – Dyspnea (10/10), consistent with presenting complaints



Case Study 1 - CPET Results

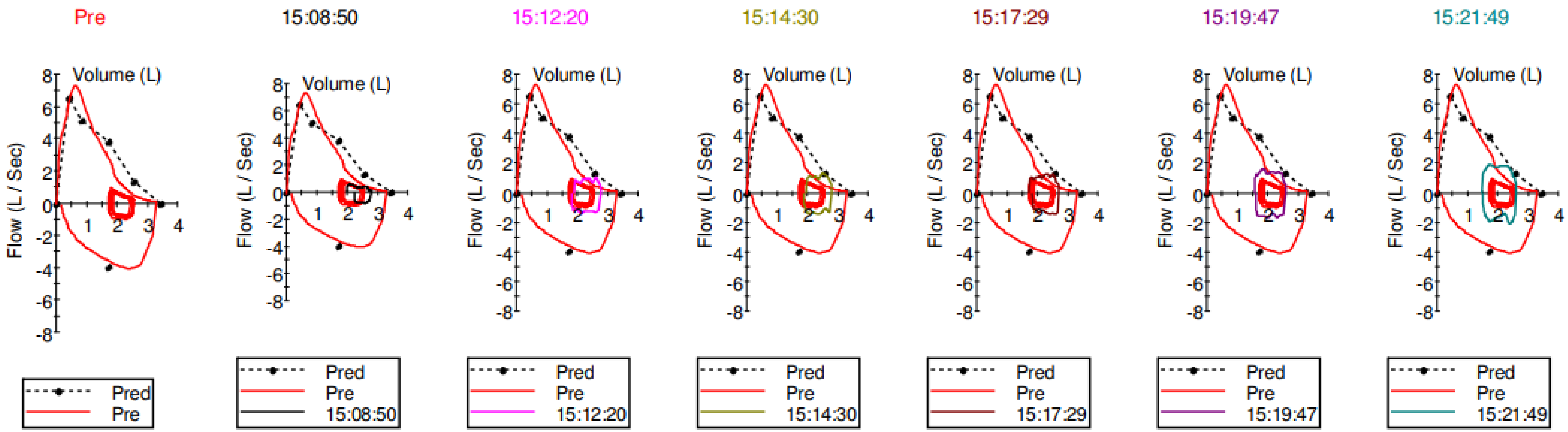
Bike-ergometer CPET with serial ExeFVL and IC maneuvers

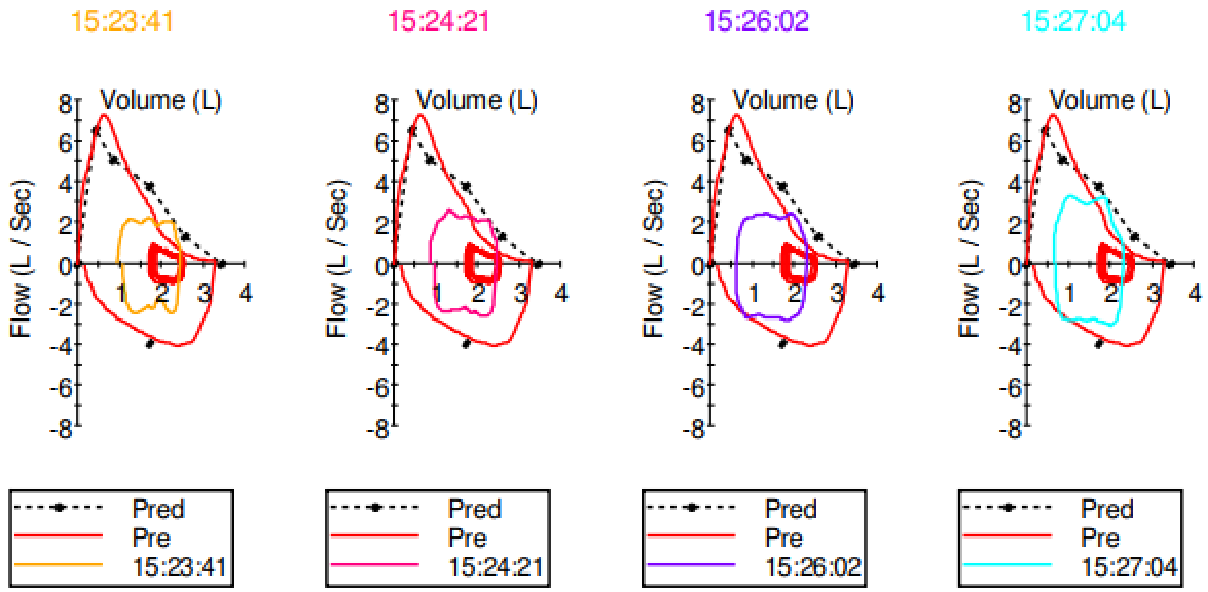
- Pre-Exe Spirometry:
  - FVC= 96%, FEV1= 92%, FEV1/FVC= 0.76 **– NORMAL (NL)**
- Exercise Test Results:
  - Functional Capacity
    - Peak Watts = 142 (154%) **- NL**,
    - VO2/WR slope= 8.5 mL/min/Watt **- NL**
    - Peak VO2 = 1879 mL/min (110%) **- NL**
    - relative VO2 = 17.3 mL/kg/min (76%) – **Mildy reduced**
    - Peak RER = 1.03
    - Anaerobic threshold = 74% **- NL**
  - Cardiovascular Response
    - HR = 96 to 170 bpm (103%) **- NL**
    - BP= 132/72 to 210/80 mmHg – **elevated (women NL sysBP <190 mmHg)**
    - Oxygen Pulse = 11.0 mL/beat (107%) – NL trajectory **- NL**
  - Ventilatory Response
    - Breathing reserve = 28% (normal >20%) **– NL**
    - Vt/IC = 57% **- NL**
  - Gas-Exchange Response
    - SpO2 = 96% to 91%RA **(Abnormal - ≥5% decrease)**
    - VE/VCO2 slope = 34.6 **- Abnormal**

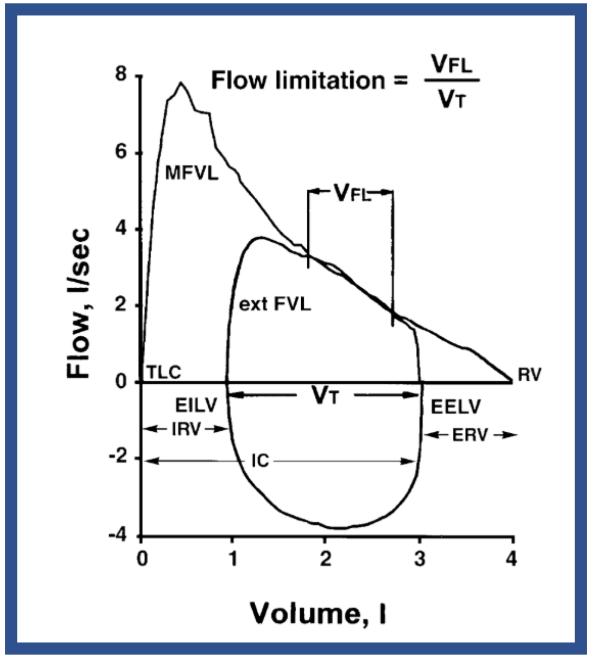


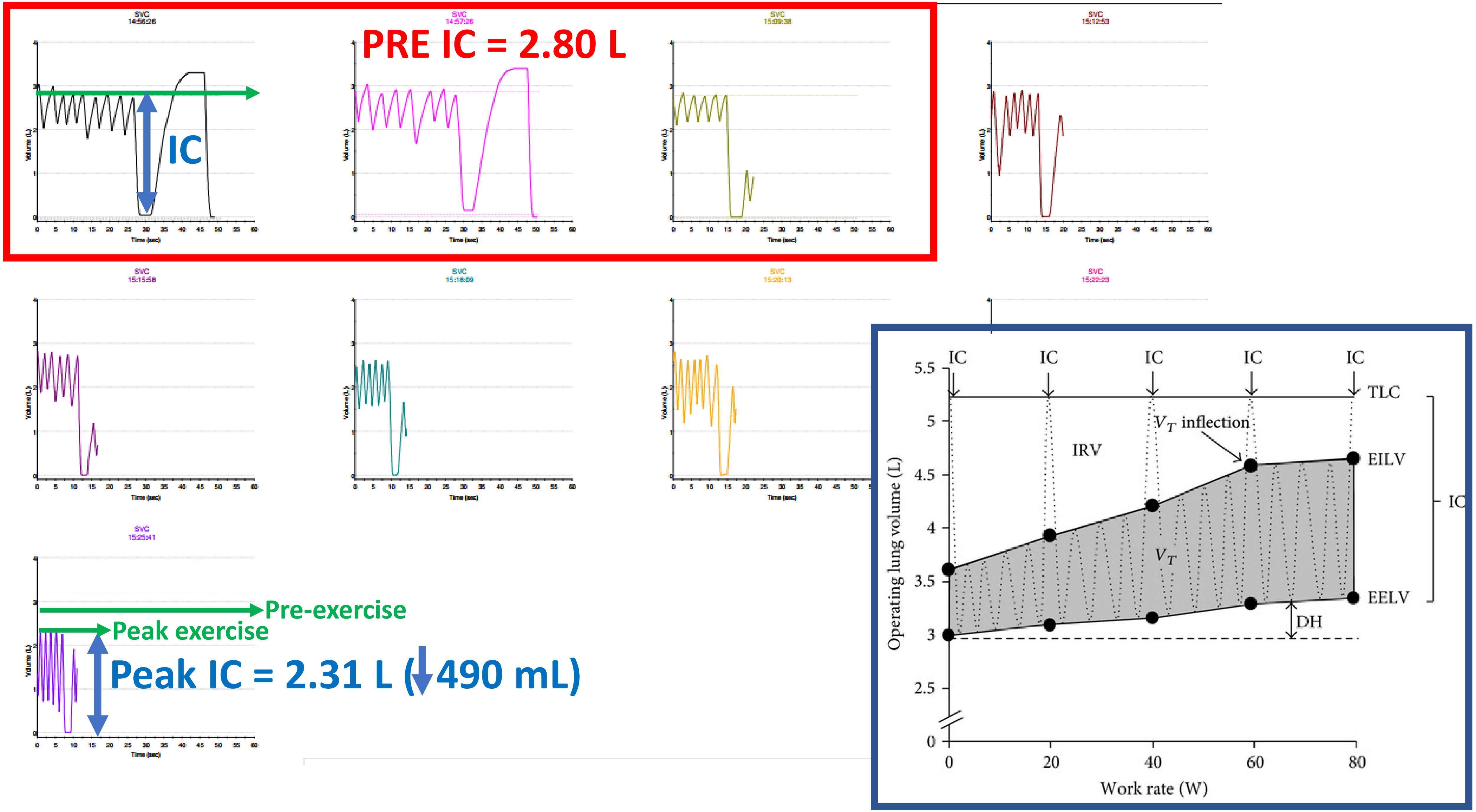
BUT, there's more to the story……….

Case Study 1 - CPET Results








PRE IC = 2.80 L
IC
Pre-exercise
Peak exercise
Peak IC = 2.31 L (↓490 mL)
IC
IC
IC
IC
IC
TLC
V_T inflection
IRV
EILV
IC
V_T
EELV
DH
Operating lung volume (L)
Work rate (W)
5.5
5
4.5
4
3.5
3
2.5
0
0
20
40
60
80

What is limiting this patient during exercise?

- 1) Significant discrepancy between %-predicted values when comparing absolute and relative VO2 (110% vs. 76% of predicted) – OBESITY is a contributor
- 2) Development of increasing expiratory flow-limitation with subsequent declines in serial inspiratory capacity maneuvers – pulmonary mechanical limitation - DYNAMIC HYPERINFLATION
- 3) Gas-exchange abnormalities (5% decrease SpO2, VE/VCO2 slope= 34.6 (Normal <30)

Case 2 – Exercise Intolerance with history of PHTN

76yo Male referred by Pulmonologist for CPET to evaluate progressive exercise intolerance with a history of Pulmonary Hypertension

Treadmill CPET Results:

- Exercise Time = 7:43 min:sec
- Peak VO_2 = 15.2 $mL \cdot kg^{-1} \cdot min^{-1}$ (61% predicted)
- VAT = 12.5 $mL \cdot kg^{-1} \cdot min^{-1}$ (3.6 METs; 50% predicted)
- RER = 1.27

- HR Response: 65 to 105 bpm (73% predicted)
- BP response: 148/60 to 189/69 mmHg
- Peak O_2 pulse = 13.1 mL/beat (83% predicted)
- VE/MVV = 0.51 (Normal <0.80)
- SpO2 response: ≥99% RA throughout exercise
- VE/VCO2 slope = 35.6 (Normal <30)

Pre-Exercise PFT Results:

FVC = 3.84 L (84%)
FEV1 = 3.20 L (109%)
FEV1/FVC ratio = 0.83
IC = 3.25 L (94%)

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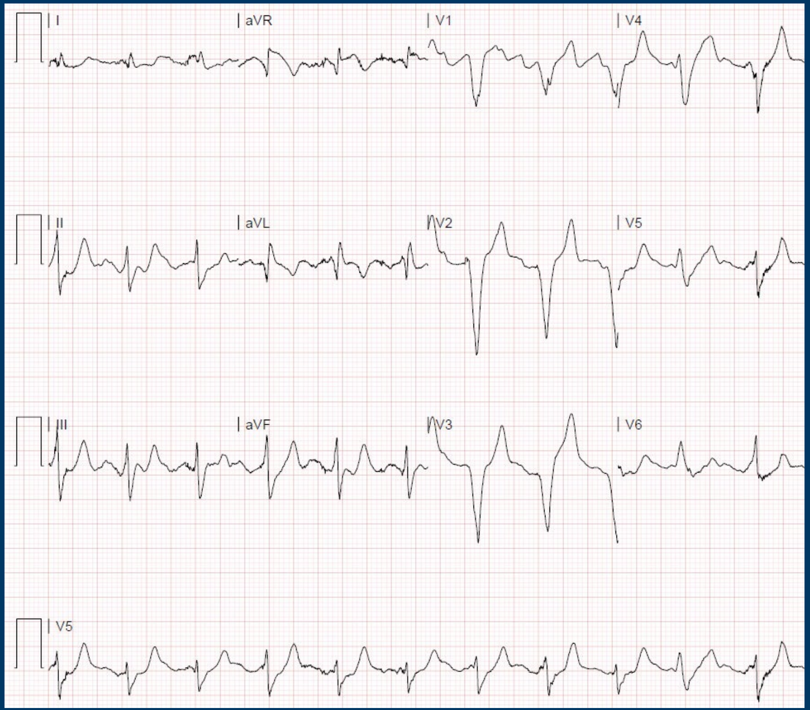
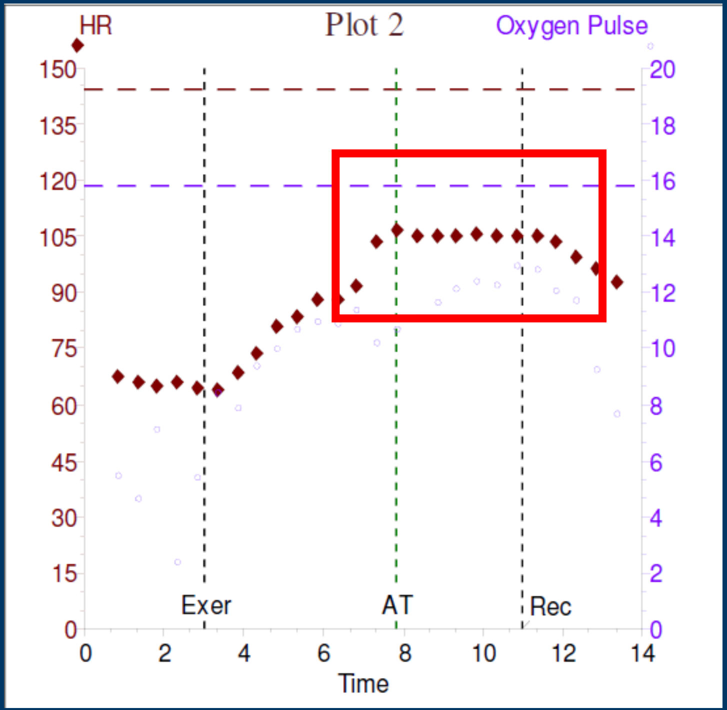
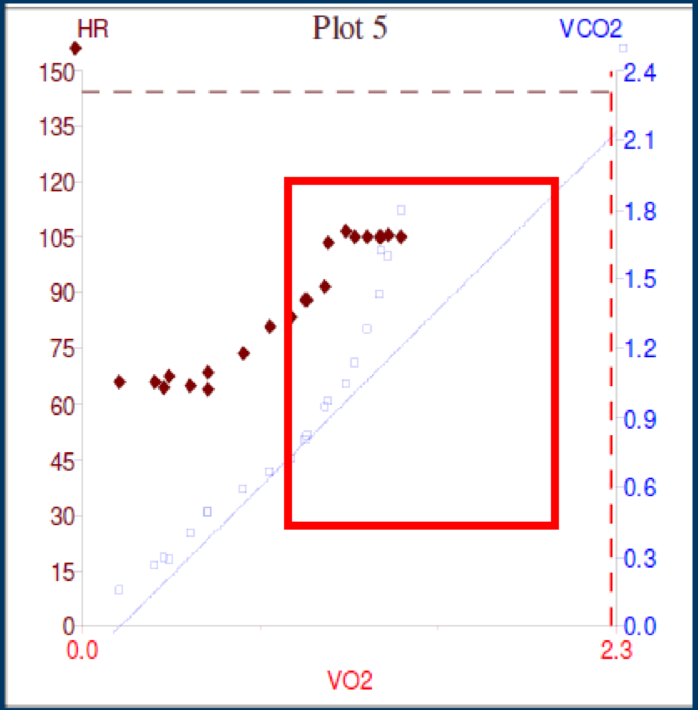
What is limiting this patient?

Case 2 – Exercise Intolerance with history of PHTN



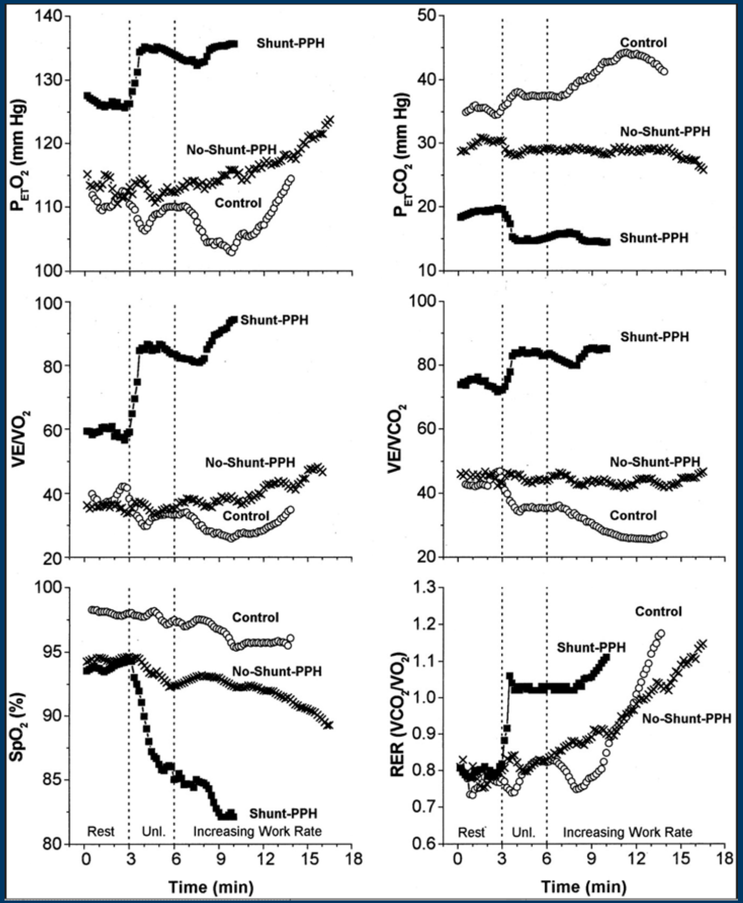




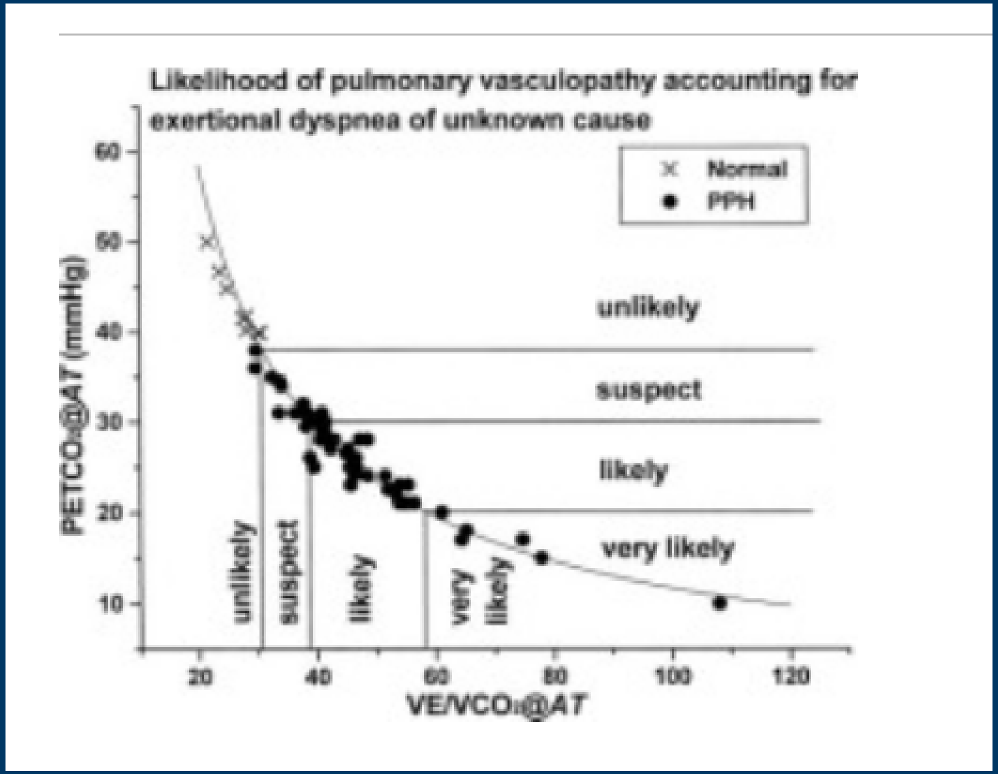
CONCLUSION:
Abnormal cardiopulmonary exercise test.
Atrial flutter with ventricular pacemaker and plateau of HR response at 4min 30 seconds into exercise.
Aerobic capacity was moderately reduced. Peak VO2 was 15.2 ml/kg/min (61 % of predicted). Anaerobic threshold was normal.
Abnormal respiratory efficiency was demonstrated (Ve/VCO2 slope=35.6), c/w the diagnosis of pulmonary hypertension.

Diagnostic Capabilities of CPET ?

Exercise-induced R-L Shunt in PPH



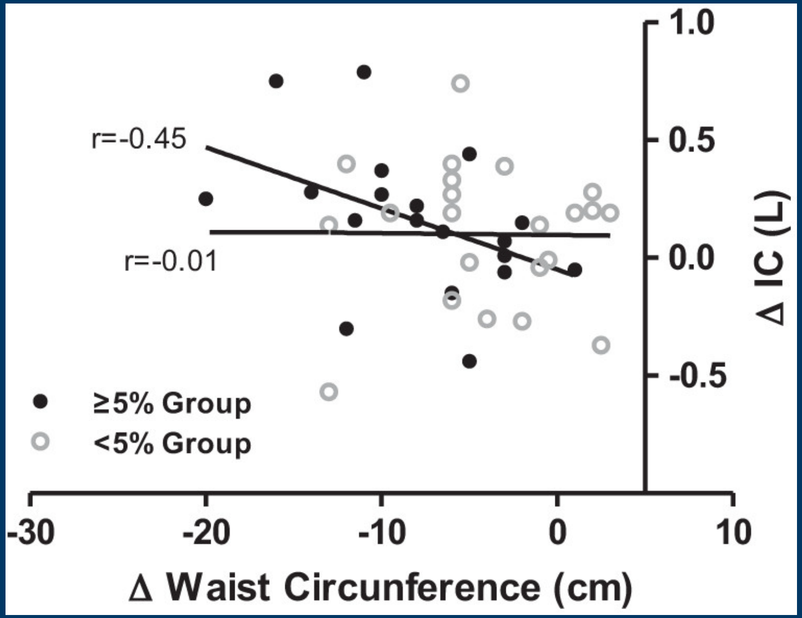
Pulmonary Hypertension

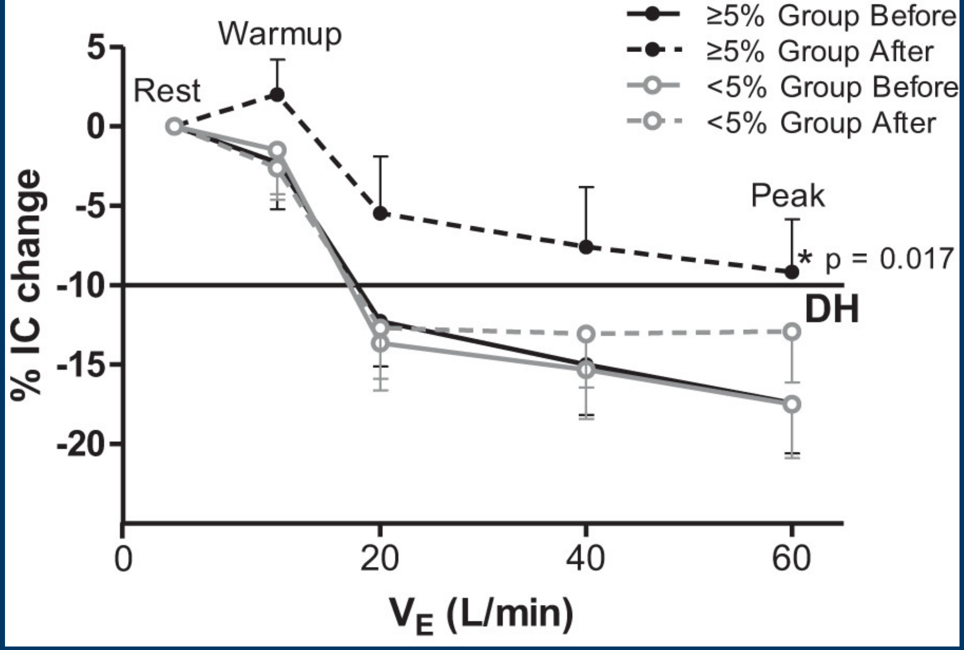


Sun XG, Circulation, 2002
Yasunobu Y, Chest, 2005

Interventions to Improve Dyspnea on Exertion

≥ 5% weight loss reduces dynamic hyperinflation and improves HRQOL in obese asthmatics





VCUHealth

Grandi Silva A, Journal of Applied Physiology, 2019

Conclusions

- The etiology of exercise intolerance is complex often multifactorial in nature
- Cardiopulmonary exercise testing permits a comprehensive and global assessment of limitations to exercise
- Evaluation of exercise response profiles permits recognition of patterns of abnormalities that may elucidate the contributors to a patient's exercise intolerance and exertional symptoms