

Evaluation of Unexplained Dyspnea

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BRIGHAM HEALTH

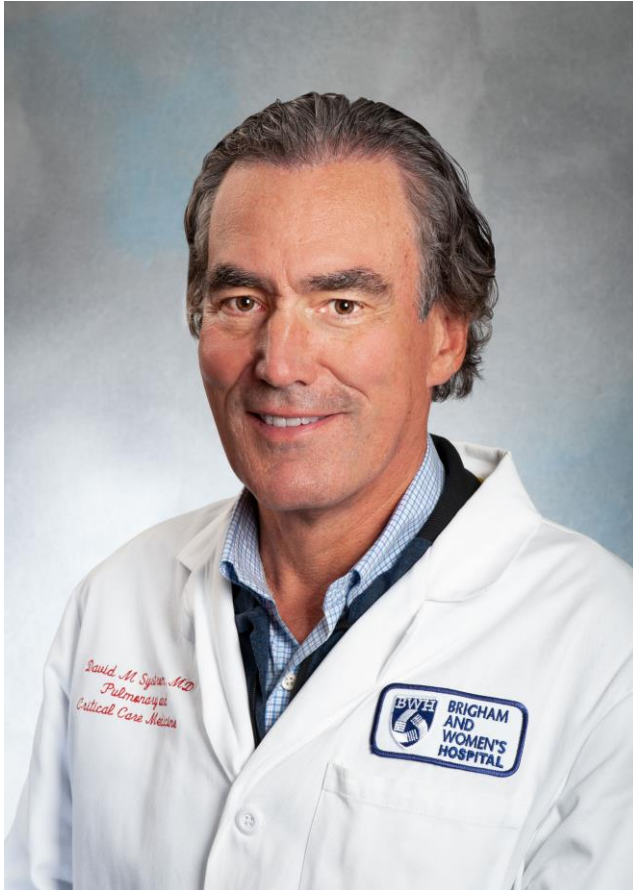


BRIGHAM AND WOMEN'S
Department of Medicine



HARVARD
MEDICAL SCHOOL
TEACHING AFFILIATE

David M Systrom, MD



- Dartmouth Medical School
- Medicine Residency @ Emory University
- PCCM Fellowship @ Mass. General Hospital
- Assistant Professor of Medicine @ HMS
 - Clinical focus: Exercise Intolerance
 - Research focus: Exercise Intolerance

Disclosures

- I have no financial disclosures

Objectives

- Use 4 case vignettes to:
 - Highlight reasons for undifferentiated dyspnea
 - Review physiologic tools available for a definitive diagnosis

Patient MF

- 21 yo male Harvard Crew
- 1.5 years SOB, especially w/ intense training, competition
- Patient and mom endorsed “noisy breathing” during exacerbations
- Rapid clearing of sx, EMT’s : “normal exam”

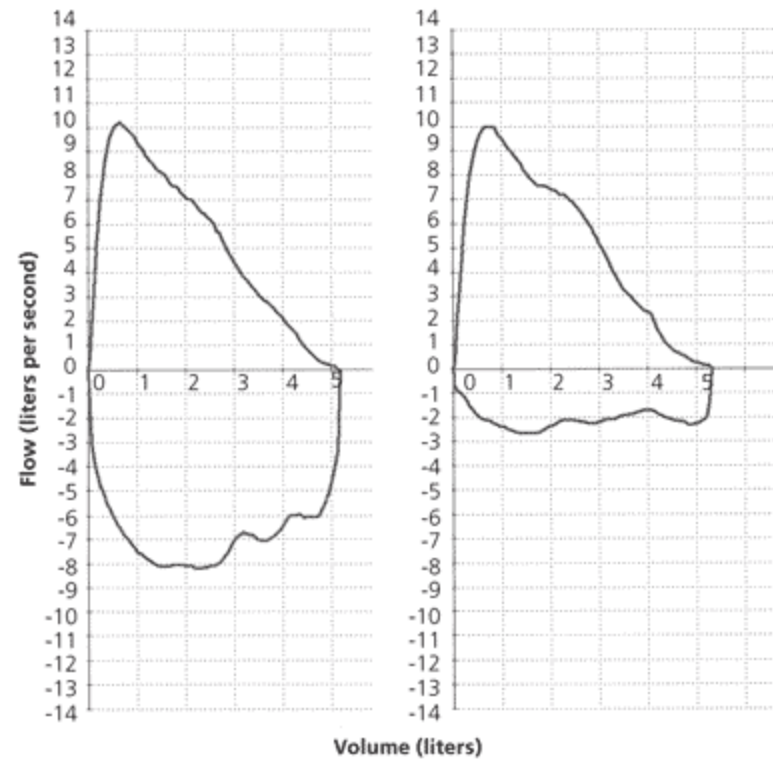
Patient MF

- “Doc make me better, we are going to the Henley”



Pt MF

- Exam: normal
- Spirometry:



Laryngoscopy figures

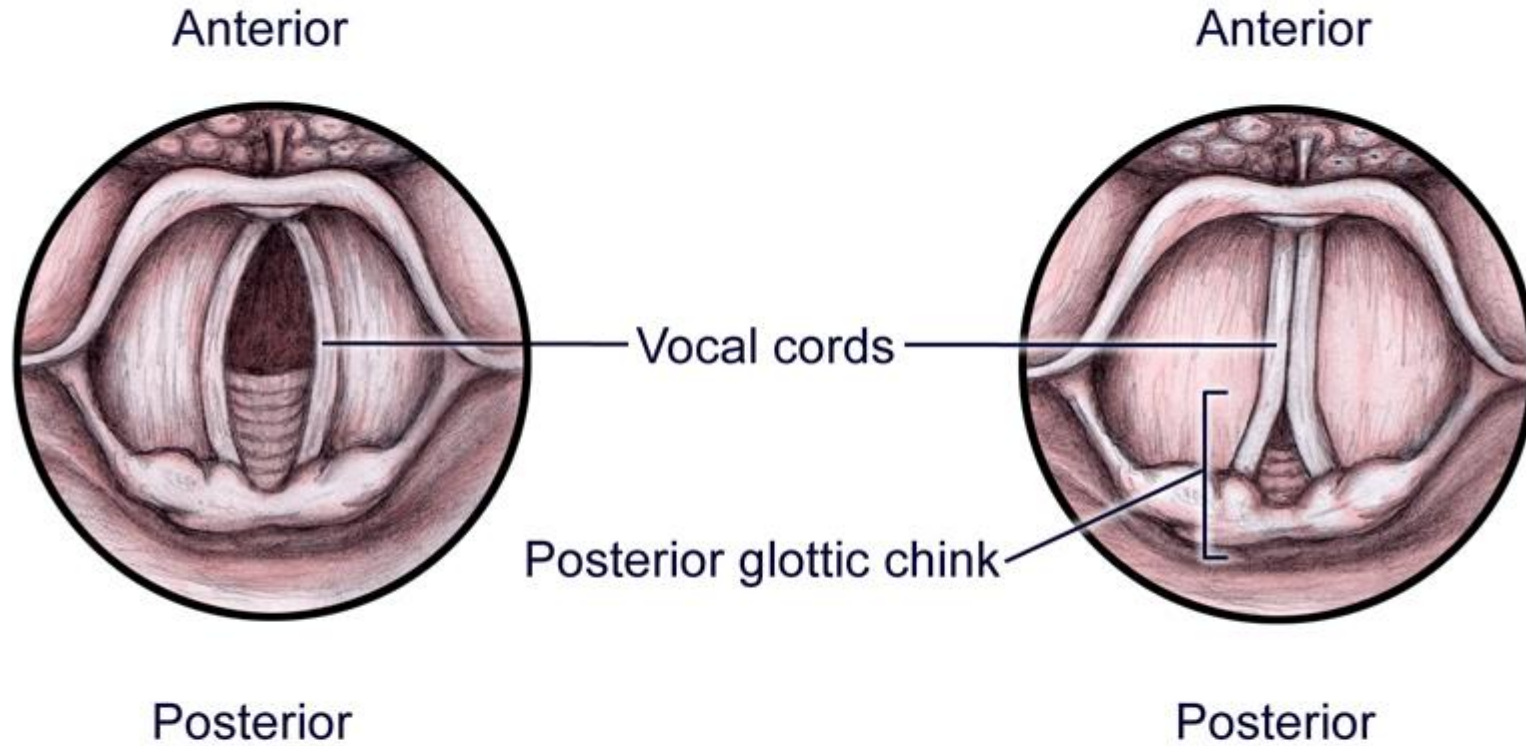


Figure C

Vocal cords during normal inspiration

Figure D

Vocal cords in a symptomatic VCD patient Note- presence of a posterior glottic chink

Vocal Cord Dysfunction

- AKA laryngeal dyskinesia
- Often young women w/ PTSD, many = conversion reaction
- Can be worsened by PND, GERD
- Key to hx is inspiratory stridor, hoarseness
- Often confused w/ asthma, methacholine challenge may help, ABG's should be normal
- Spirometry: flattened inspiratory F-V loop
- Confirmation w/ direct laryngoscopy: panting, full exhalation: forced inspiration, exercise... ..inappropriate closure of glottis during inspiration
- Treatment: voice training, SSRI

Pt WL

- 51 YO M, mildly obese
- Previously 35 min Elliptical, 4 d /week, TM 4.4 mph, 4 deg, 15 min.
- 3 mos. Previously, hanging an AC unit out a window, leaning over a windowsill, and had sudden R anterior sharp CP, persistent R shoulder pain and SOB since, immediate orthopnea
- No persistent cough, wheeze, F, C, sweat, B sx.

Pt WL

SPIROMETRY (BTPS)

		Predicted		Pre-BD	
		Mean	95% CI	Actual	%Pred
FVC	(Lts)	5.24	4.12	2.30	44
FEV1	(Lts)	4.14	3.30	1.70	41
FEV6	(Lts)	5.19	4.23	2.28	44
FEV1/FVC	(%)	79	71	74	94

LUNG VOLUMES (PLETHYSMOGRAPHY)

TLC	(Lts)	7.41	5.80	4.68	63
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DIFFUSING CAPACITY

DLCO Unc	(mL/min/mmHg)	32.71	22.69	25.85	79
DLCO Corr (Hb)	(mL/min/mmHg)	32.71	22.69	25.85	79
VA@BTPS	(Lts)	7.41	6.26	3.93	53
DL/VA	(%)	4.43	3.50	6.58	149

RESPIRATORY MUSCLE STRENGTH

MIP		89	34	38
MEP		134	68	51

Pt WL



Pt WL



Respiratory Muscle Weakness

- Acute or chronic DOE, immediate orthopnea
- Usually B diaphragmatic dysfxn, but unilateral plus other can > SOB
- Diagnosis:
 - Restrictive defect may be mild
 - VC upright > supine (10% fall), MIP
 - CT chest > r/o mass, LAD
 - Phrenic nerve conduction, diaphragmatic EMG
- Treatment
 - Time, e.g., trauma, CABG
 - Weight loss
 - Elevate HOB
 - PSG: look for hypopneas > BiPAP
 - Inspiratory muscle training
 - IVIg, steroids

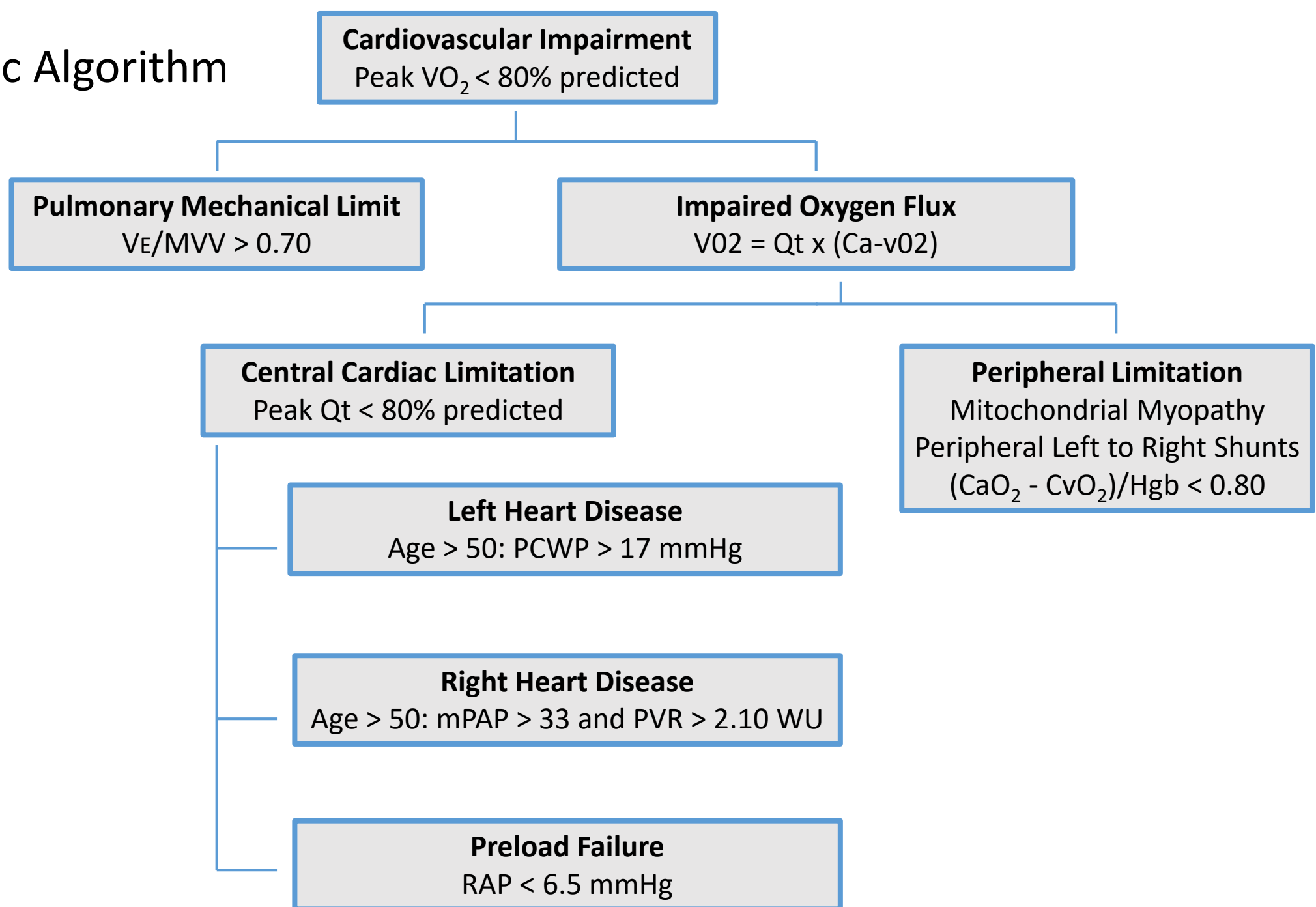
Pt MR

- 61 yo running Shoe Co Exec
- Two-year decline in running splits 6>8 min miles due to SOB
- No immediate orthopnea, myalgias, lightheadedness
- Exam routine labs normal
- Spirometry, TTE, CT chest, cardiac stress normal
- Invasive CPET:

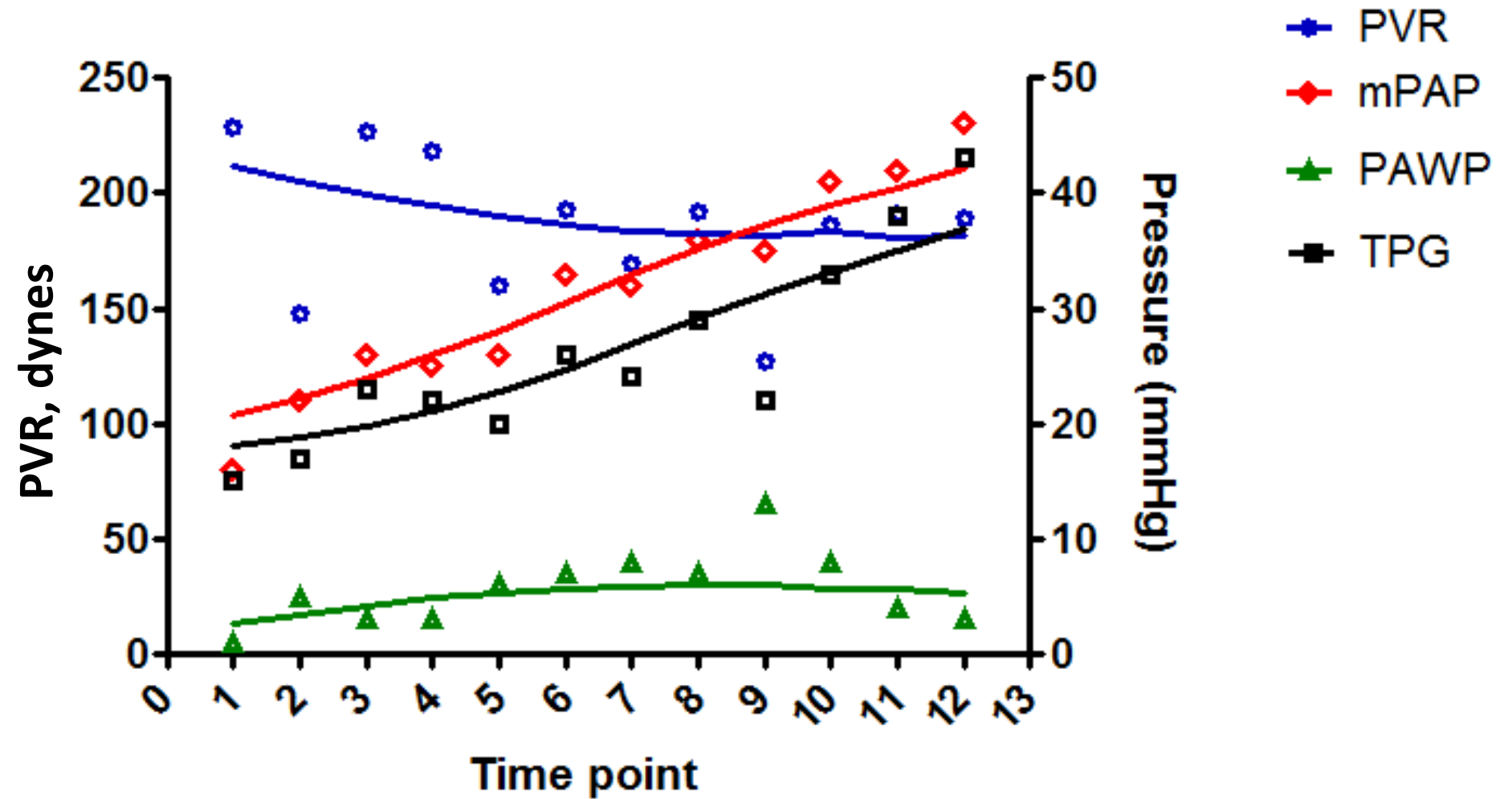
Cardiopulmonary Exercise Test



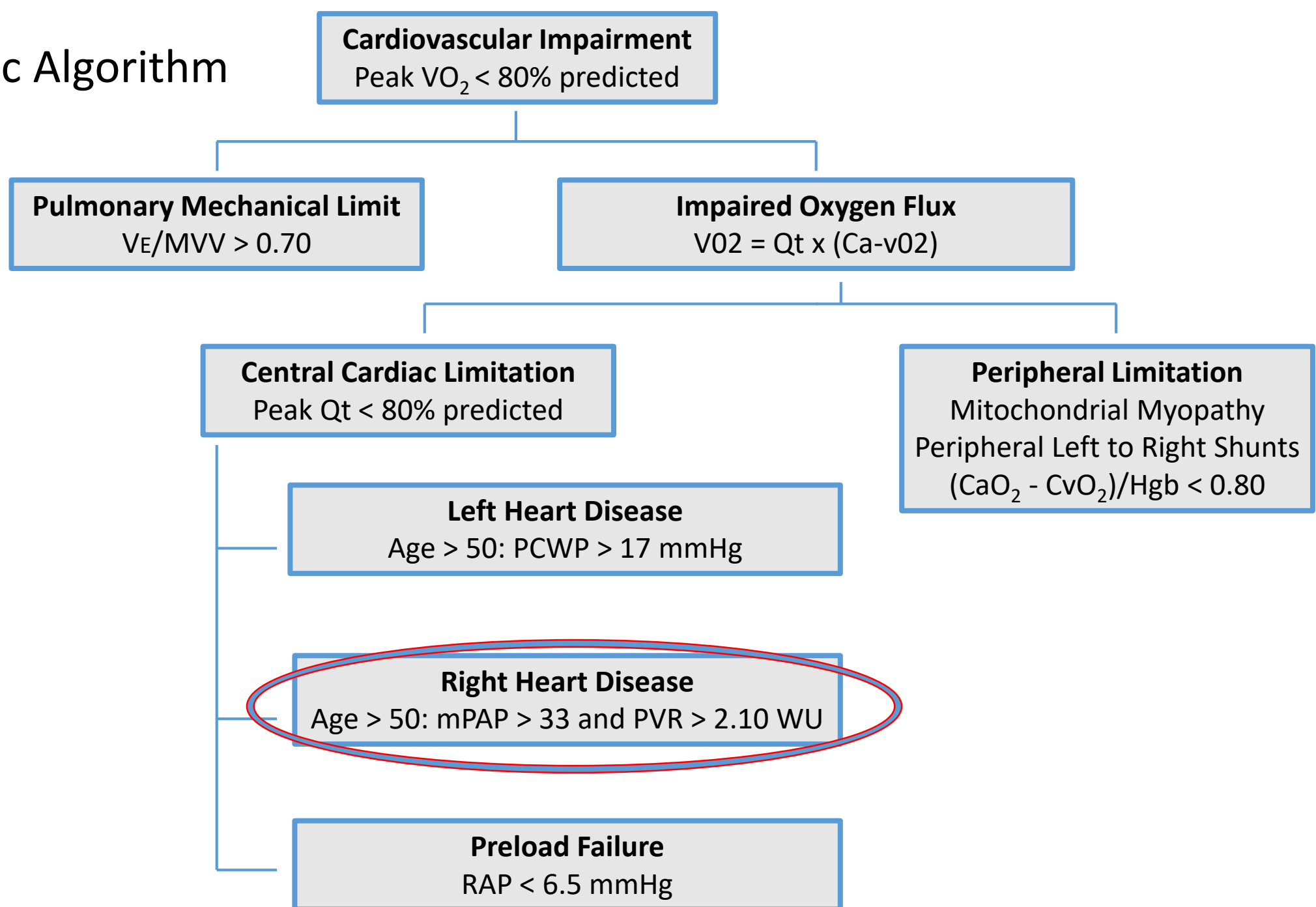
iCPET Diagnostic Algorithm



Pt MR



iCPET Diagnostic Algorithm



Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

Exercise-Induced Pulmonary Arterial Hypertension

James J. Tolle, Aaron B. Waxman, Teresa L. Van Horn, Paul P. Pappagianopoulos
and David M. Systrom

Circulation 2008;118:2183-2189; originally published online Nov 3, 2008;

DOI: 10.1161/CIRCULATIONAHA.108.787101

Exercise PH

- Presents w/ unexplained dyspnea
- aCPET: Intermediate exercise phenotype between normal and resting PAH
- ? Early disease vs stable variant
- Missed by TTE and resting RHC
- Ambrisentan responsive, ? Others
- Need clinical trials

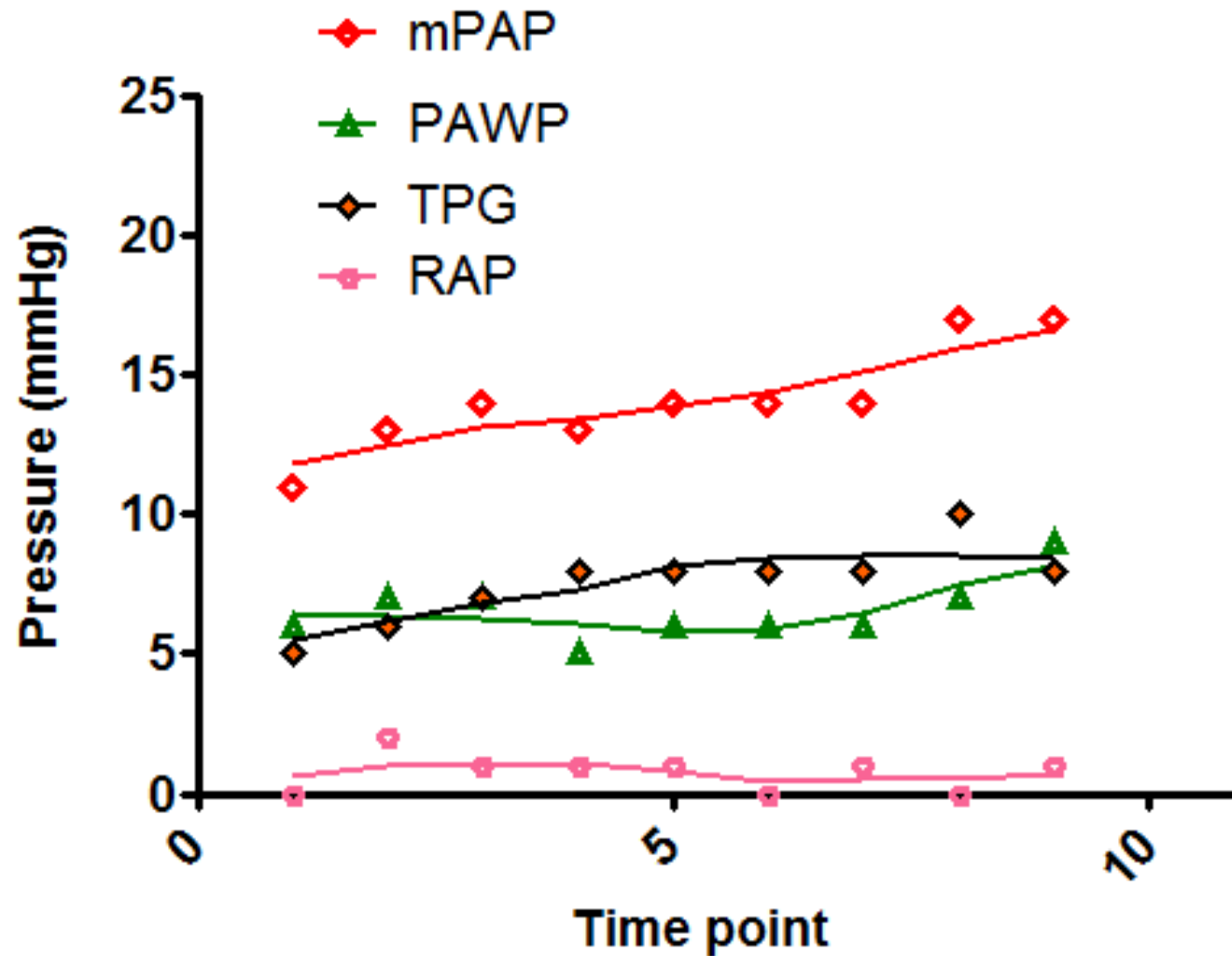
Case CG

- 42 yo F
- Well until acute COVID 3/21: cough and fever > 2 week hospitalization, ICU, no intubation
- At D/C and one yr post: fatigue, post exertional malaise, non refreshing sleep, brain fog, orthostatic intolerance, 1 FOS DOE
- Exam, routine labs, TTE, CT chest: all normal

CG: Mildly depressed V02 peak
Normal pulmonary blood flow

•	-----		
•		Predicted	Measured % Pred
•	-----		
•	Peak VO2 (mL/min)	1595	1173 74%
•	Cardiac Output (L/min)	11.4	10.6 93%

CG: iCPET>Preload failure



CG: Impaired Systemic O₂ extraction

• Time	Watts	VO2	Qt	SvO2	HR	SV	BP
• -----							
• REST	0	228	4.15	66.4	61	68.0	96/67
• -----							
• -----							
• PEAK	115	1173	10.57	37.7	131	80.7	111/69

CG: Skin Bx for SFN

9/20/2021

Reported: 10/4/2021 13:15

Results To:

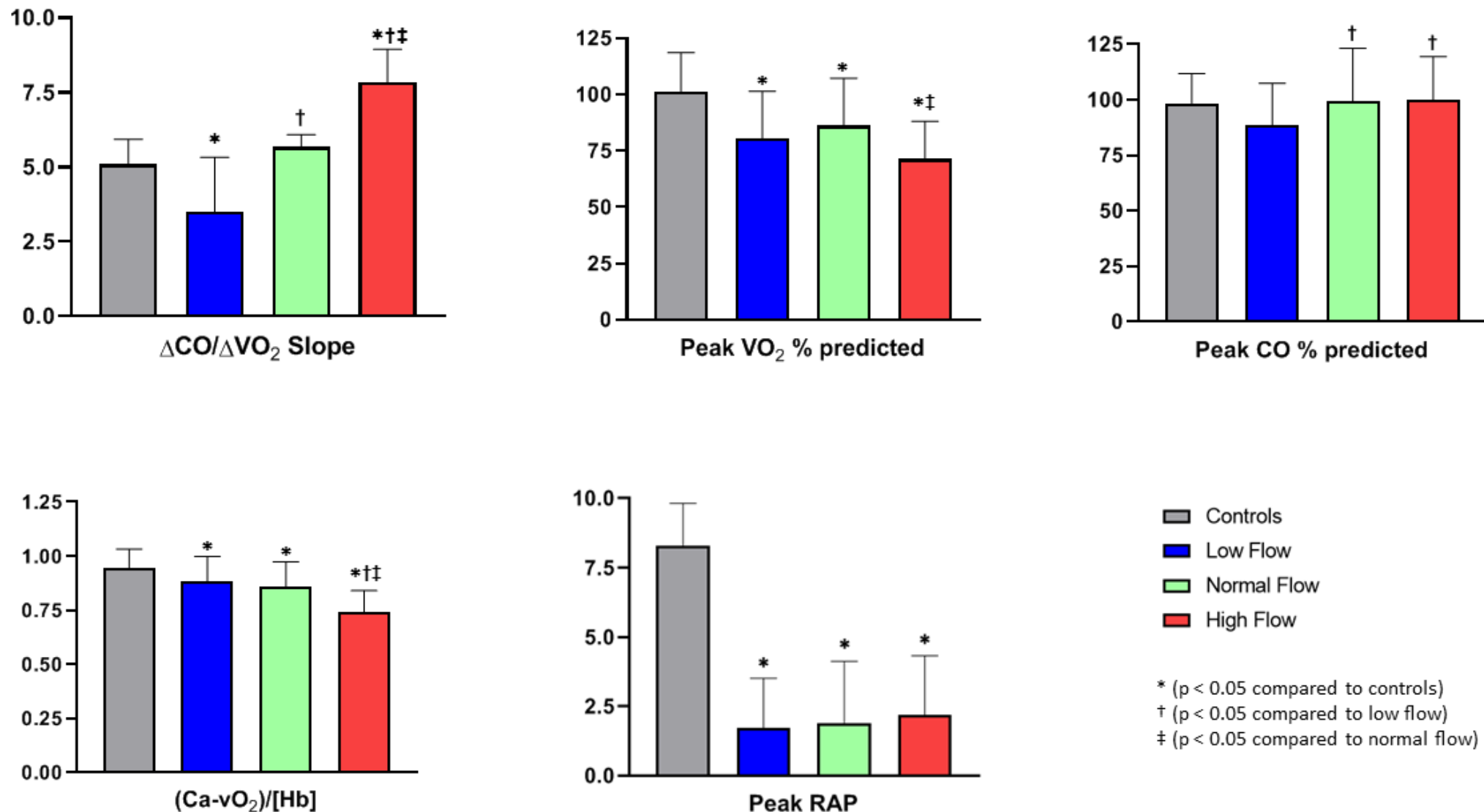
David M Systrom MD

FINAL PATHOLOGIC DIAGNOSIS:

SKIN (STANDARD LOWER-LEG SITE), PUNCH BIOPSY:

Morphometric quantitation of epidermal nerve endings yielded epidermal neurite density (END) of 117 neurites/mm² skin surface area, at **less than the 1st centile**. ENDs d 5th centile of predicted are interpreted as pathologically confirming small-fiber axonopathy in clinically suspected patients.

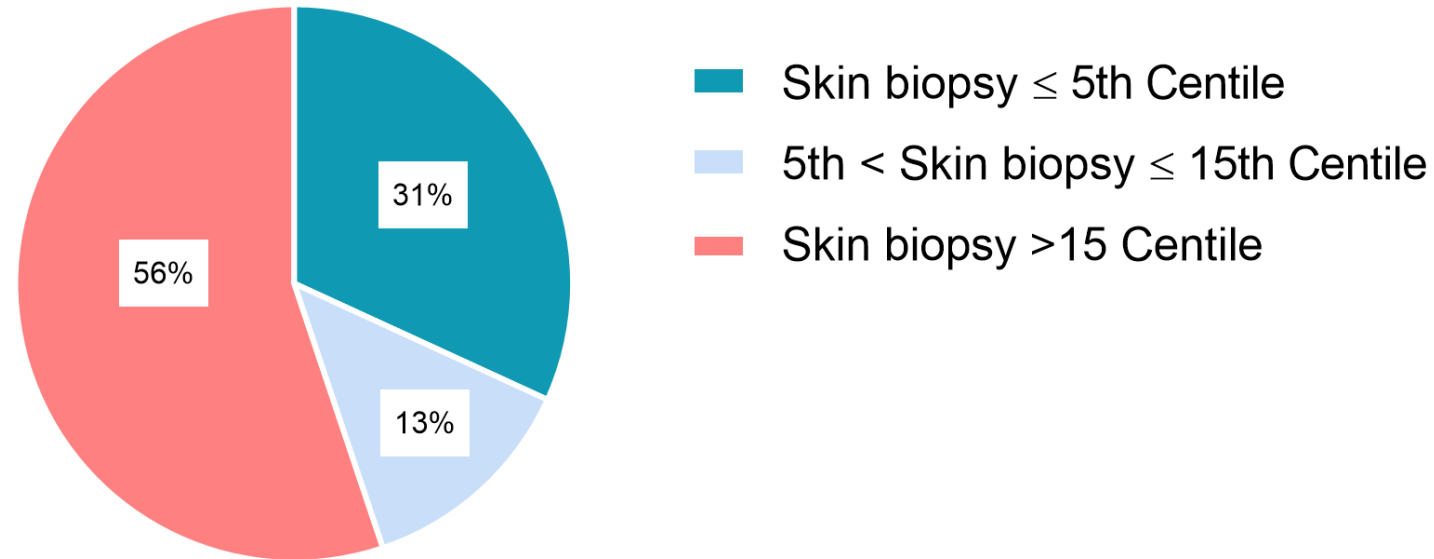
High flow v. low flow in ME/CFS



Joseph P, Arevalo C, Oliveira RKF, Faria-Urbina M, Felsenstein D, Oaklander AL, Systrom DM. Insights From Invasive Cardiopulmonary Exercise Testing of Patients With Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. Chest. 2021 Feb 10:S0012-3692(21)00256-7. doi: 10.1016/j.chest.2021.01.082.

Small Fiber Neuropathy in ME/CFS

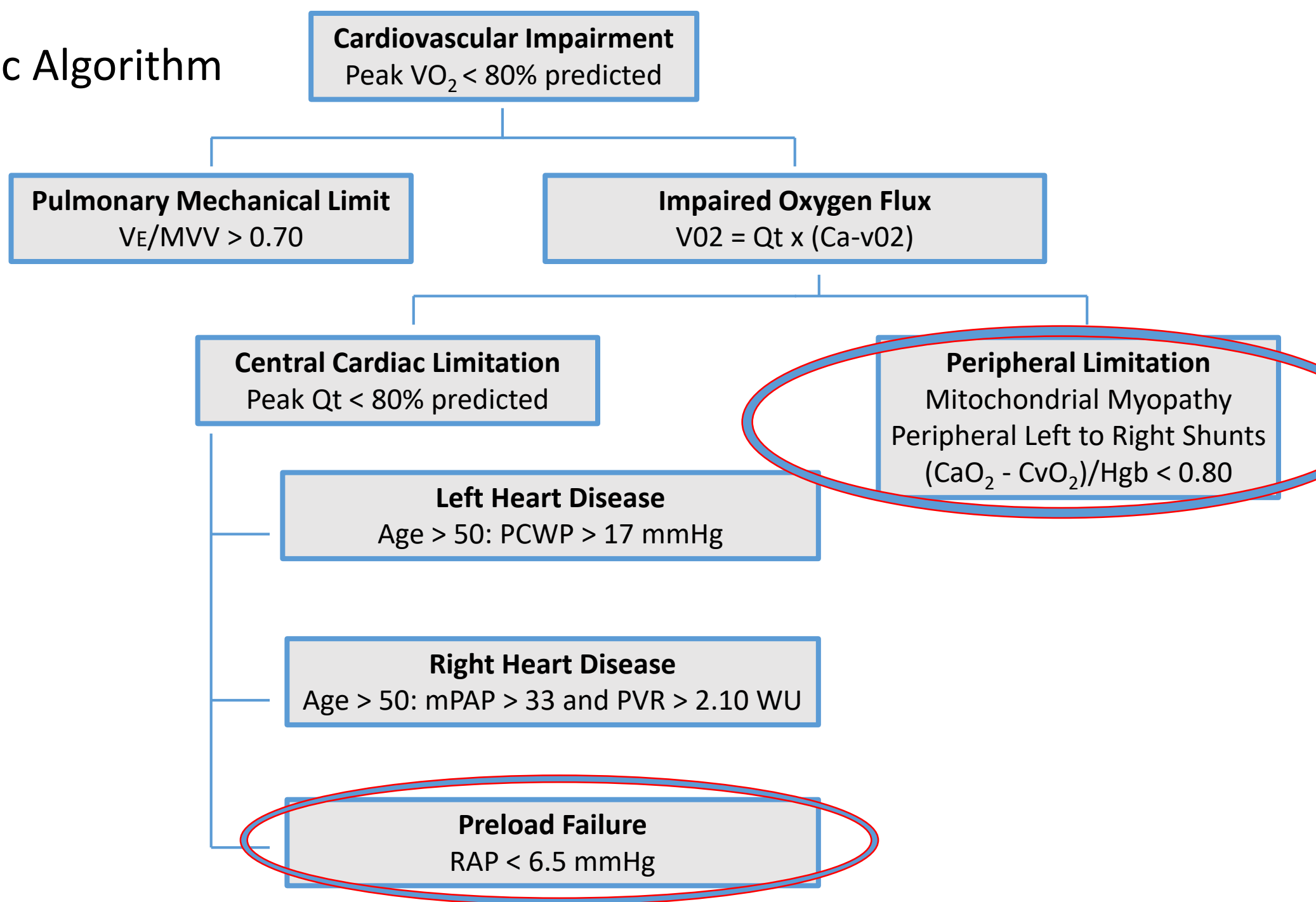
Skin biopsy in ME/CFS



Total=160

Joseph P, Arevalo C, Oliveira RKF, Faria-Urbina M, Felsenstein D, Oaklander AL, Systrom DM.
Insights From Invasive Cardiopulmonary Exercise Testing of Patients With Myalgic Encephalomyelitis/Chronic Fatigue
Syndrome. Chest. 2021 Feb 10:S0012-3692(21)00256-7. doi: 10.1016/j.chest.2021.01.082.

iCPET Diagnostic Algorithm



Case CG

Follow-up

- started pyridostigmine 30 mg po BID, graded exercise
- fatigue, OI and DOE “85% better”

ME/CFS & Long COVID

- Female predominance, fatigue, PEM, non-refreshing sleep, brain fog, lightheadedness and DOE
- Routine w/u often neg.
- AFT including skin bx for SFN useful
- iCPET > neurovascular dysregulation & hyperventilation
- Rx salt and H₂O load, compression stockings, POTS drugs, IVIg, graded exercise

Take-Home Messages

- a. Unexplained dyspnea is defined as un or under-explained sx after a thorough hx, exam, routine labs, full PFT's, TTE and chest radiography when appropriate
- b. Additional testing might include an ENT eval, MTC, MIP's
- c. iCPET can rule in or out exercise-induced PH, CHF, preload failure and mitochondrial dysfunction

Board Questions

18 yo F presents w/ two years of DOE and subjective wheezing. Exam in office is normal. PEFr in the office and field is repeatedly normal. SABA and ICS/LABA have not helped. The next step should be:

- a. Escalation of asthma controllers, e.g., tiotropium
- b. CT chest
- c. TTE
- d. Cardiopulmonary exercise testing
- e. Methacholine challenge

Board Questions

18 yo F presents w/ two years of DOE and subjective wheezing. Exam in office is normal. PEFR in the office and field is repeatedly normal. SABA and ICS/LABA have not helped. The next step should be:

- a. Escalation of asthma controllers, e.g., tiotropium
- b. CT chest
- c. TTE
- d. Cardiopulmonary exercise testing
- e. **Methacholine challenge**

Board Questions

23 yo F presents w/ 18 mos of DOE following acute COVID. Her DDx includes:

- a. eiPAH
- b. Preload failure
- c. Mt myopathy
- d. All of the above
- e. b&c

Board Questions

- 23 yo F presents w/ 18 mos of DOE and episodic lightheadedness following acute COVID. Her DDx includes:
 - a. eiPAH
 - b. Preload failure
 - c. Mt myopathy
 - d. All of the above
 - e. b&c

References

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- Functional impact of exercise pulmonary hypertension in patients with borderline resting pulmonary artery pressure. Oliveira RKF Faria Urbina M, Maron BA, Santos M, Waxman AB, Systrom DM. *Pulm Circ* 2017. DOI: 10.1177/2045893217709025
- Maron BA, Cockrill BA, Waxman AB, Systrom DM. The invasive cardiopulmonary exercise test. *Circulation*. 2013;127:1157-1164
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- Singh I, Joseph P, Heerdt PM, Cullinan M, Lutchmansingh DD, Gulati M, Possick JD, Systrom DM, Waxman AB. Persistent Exertional Intolerance After COVID-19: Insights From Invasive Cardiopulmonary Exercise Testing. *Chest*. 2022 Jan;161(1):54-63. doi: 10.1016/j.chest.2021.08.010. Epub 2021 Aug 11. PMID: 34389297; PMCID: PMC8354807.