Circulatory Dysfunction in ME/CFS

David M Systrom, MD
Associate Physician
Pulmonary & Critical Care Medicine
Mass. General Brigham

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HARVARD MEDICAL SCHOOL

Circulatory dysfunction in ME/CFS

- Invasive Cardiopulmonary Exercise Test (iCPET)
- Preload failure
- Impaired systemic 02 extraction

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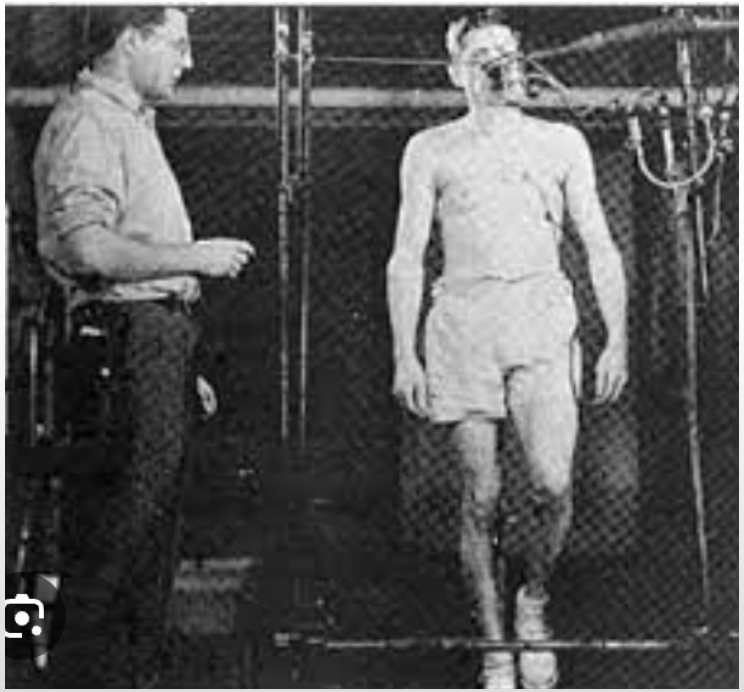
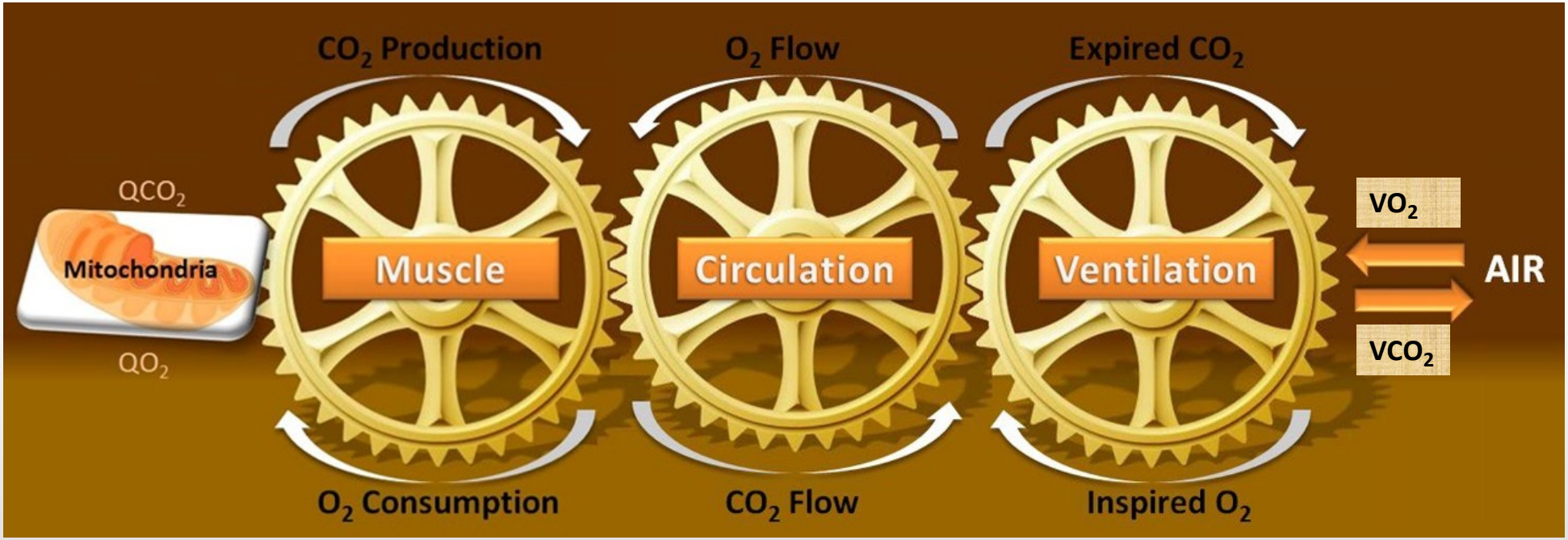
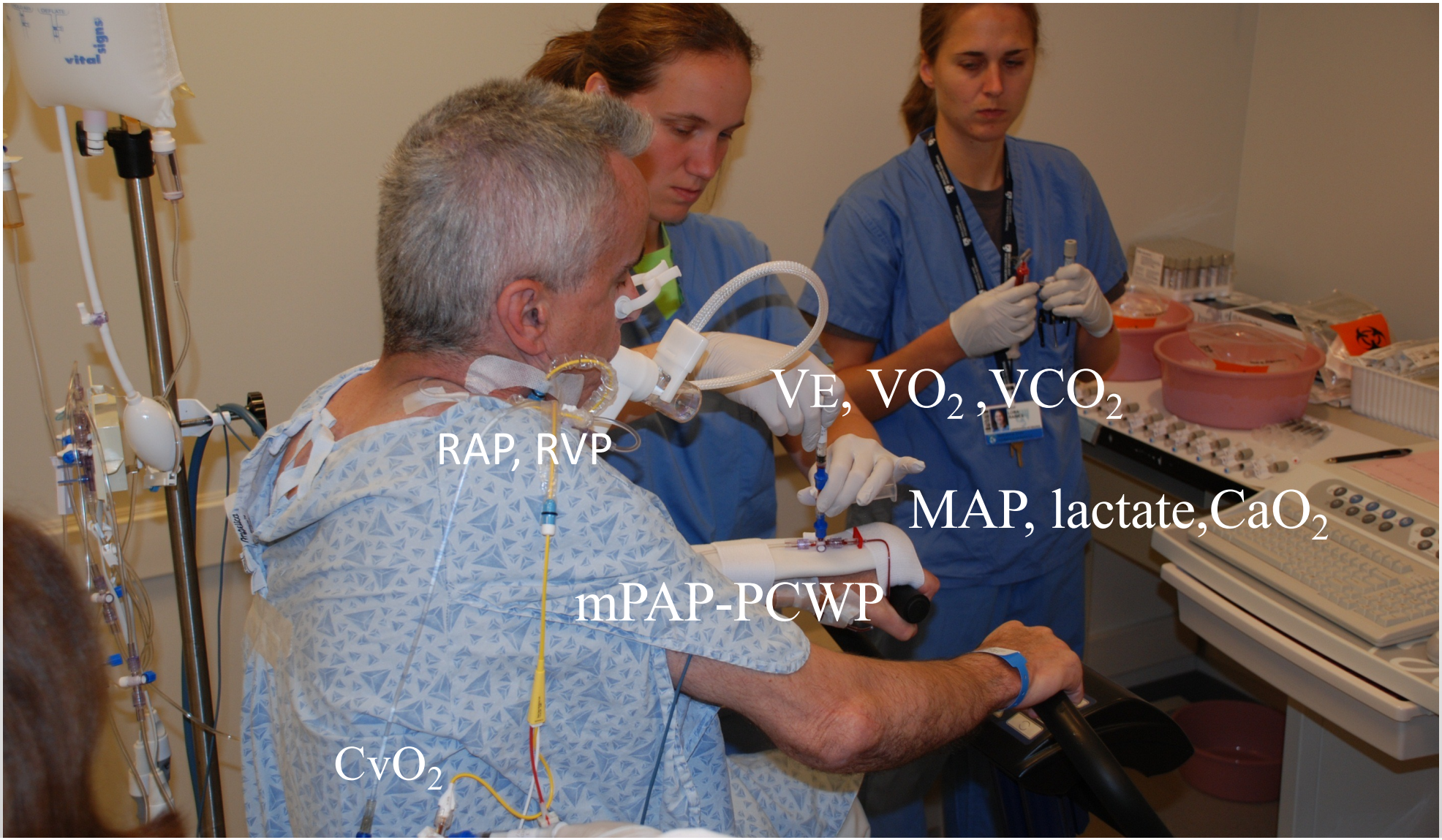
Harvard Fatigue Lab
1927-47



Exercise


CO_2 Production
O_2 Flow
Expired CO_2
QCO_2
Mitochondria
QO_2
Muscle
Circulation
Ventilation
VO_2
AIR
VCO_2
O_2 Consumption
CO_2 Flow
Inspired O_2

Invasive Cardiopulmonary Exercise Test

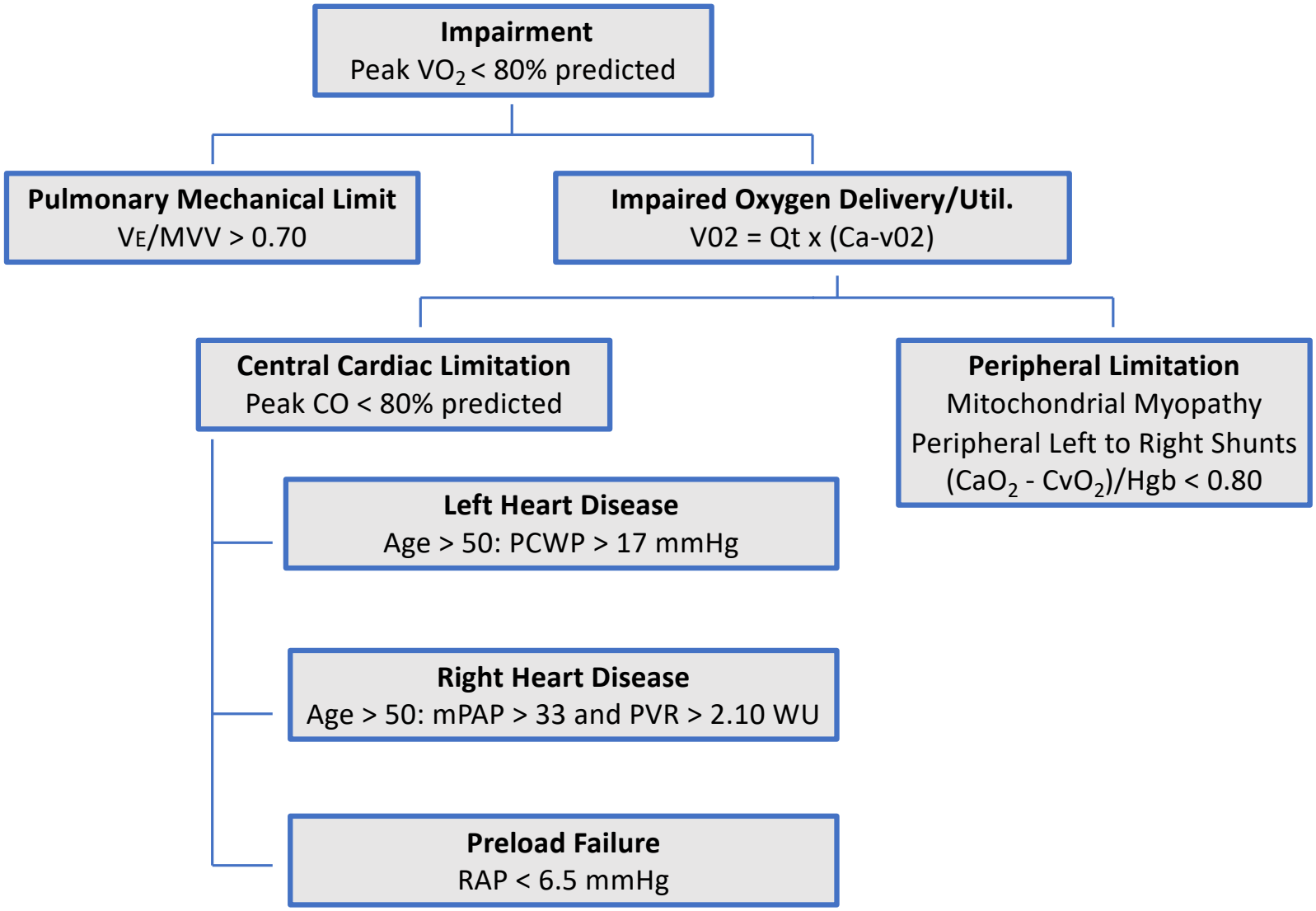

vital signs
VE, VO_2 , VCO_2
RAP, RVP
MAP, lactate,CaO_2
mPAP-PCWP
CvO_2

Fick Principle

$$V02 = Qc \times (Ca\text{-}v02)$$

$$Qc = V02/(Ca\text{-}v02)$$

Adolf Fick (1829–1901)


Impairment
Peak VO_2 < 80% predicted
Pulmonary Mechanical Limit
V_E/MVV > 0.70
Impaired Oxygen Delivery/Util.
V02 = Qt x (Ca-v02)
Central Cardiac Limitation
Peak CO < 80% predicted
Peripheral Limitation
Mitochondrial Myopathy
Peripheral Left to Right Shunts
(CaO_2 - CvO_2)/Hgb < 0.80
Left Heart Disease
Age > 50: PCWP > 17 mmHg
Right Heart Disease
Age > 50: mPAP > 33 and PVR > 2.10 WU
Preload Failure
RAP < 6.5 mmHg

Circulatory dysfunction in ME/CFS

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- Preload failure

ORIGINAL RESEARCH

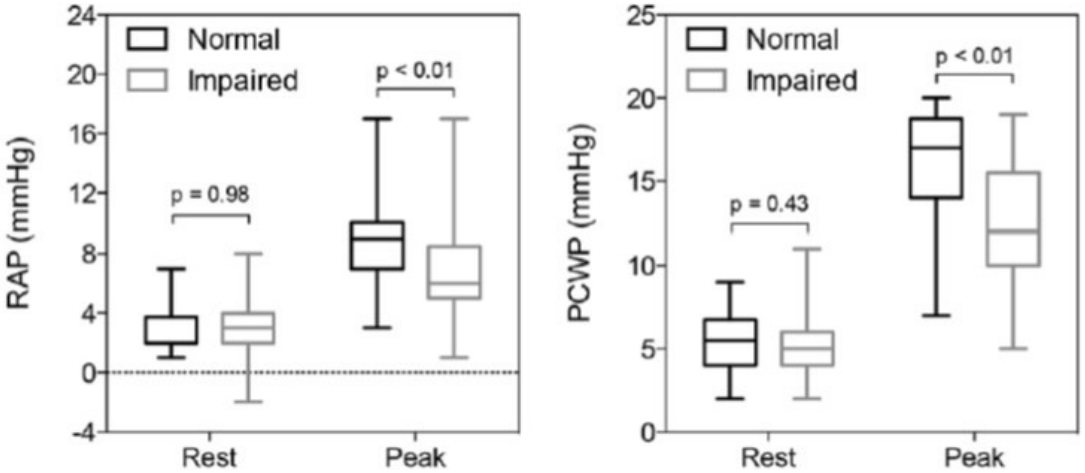
Unexplained exertional dyspnea caused by low ventricular filling pressures: results from clinical invasive cardiopulmonary exercise testing

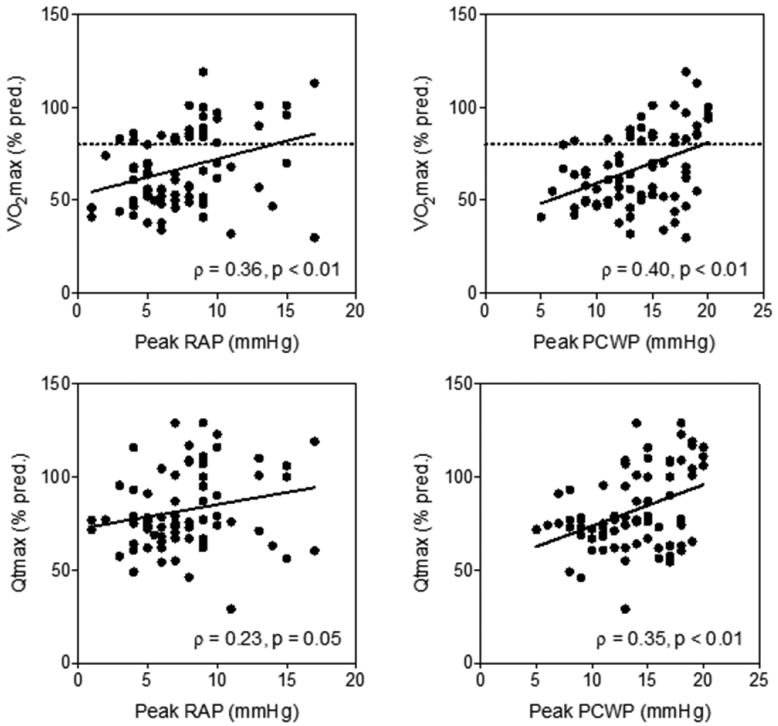
William M. Oldham,[1,2,3] Gregory D. Lewis,[3,4] Alexander R. Opotowsky,[2,3,5] Aaron B. Waxman,[1,2,3] David M. Systrom[1,2,3]

[1]Pulmonary and Critical Care Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA; [2]Heart and Vascular Center, Brigham and Women's Hospital, Boston, Massachusetts, USA; [3]Department of Medicine, Harvard Medical School, Boston, Massachusetts, USA; [4]Pulmonary and Critical Care Unit and Cardiology Division, Medical Services, Massachusetts General Hospital, Boston, Massachusetts, USA; [5]Department of Cardiology, Boston Children's Hospital, and Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA

Pulmonary Circulation. March 2016:55-62.
doi:10.1086/685054

Preload Failure





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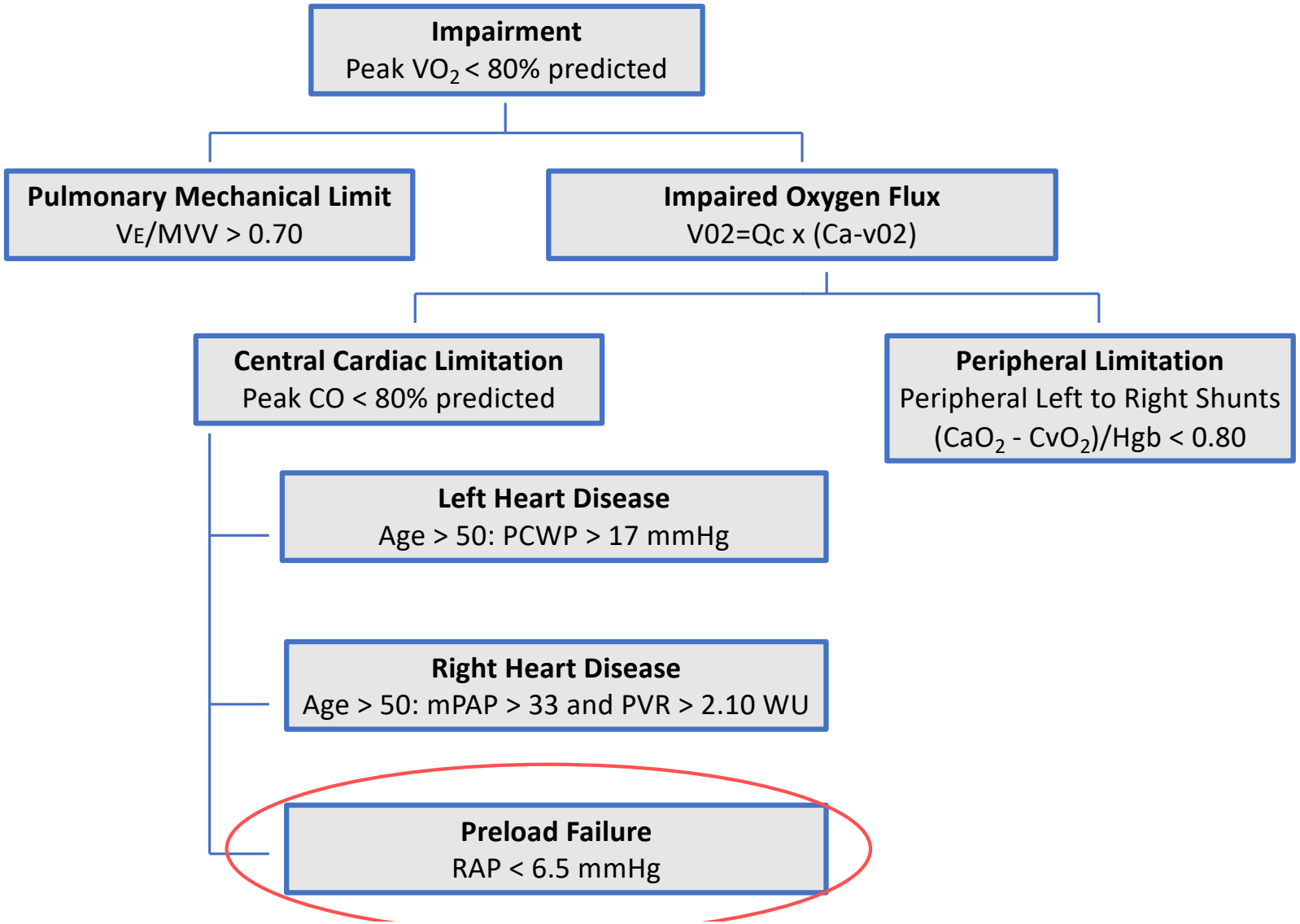
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- Impaired systemic 02 extraction

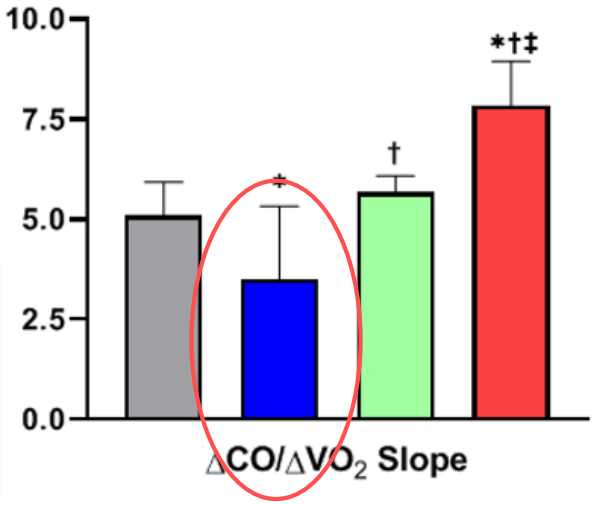
Insights From Invasive Cardiopulmonary Exercise Testing of Patients With Myalgic Encephalomyelitis/Chronic Fatigue Syndrome

Phillip Joseph, MD; Carlo Arevalo, MD; Rudolf K. F. Oliveira, MD, PhD; Mariana Faria-Urbina, MD; Donna Felsenstein, MD; Anne Louise Oaklander, MD, PhD; and David M. Systrom, MD

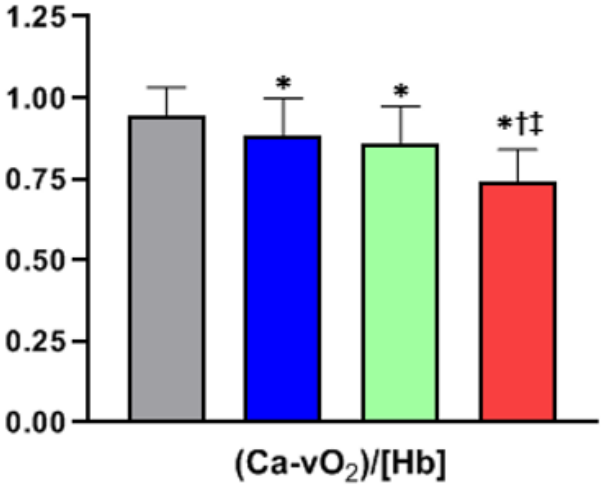
Chest. 2021 Aug;160(2):642-651. doi: 10.1016/j.chest.2021.01.082. Epub 2021 Feb 10. PMID: 33577778.

Low flow = preload failure

V02=Qc x (Ca-v02)



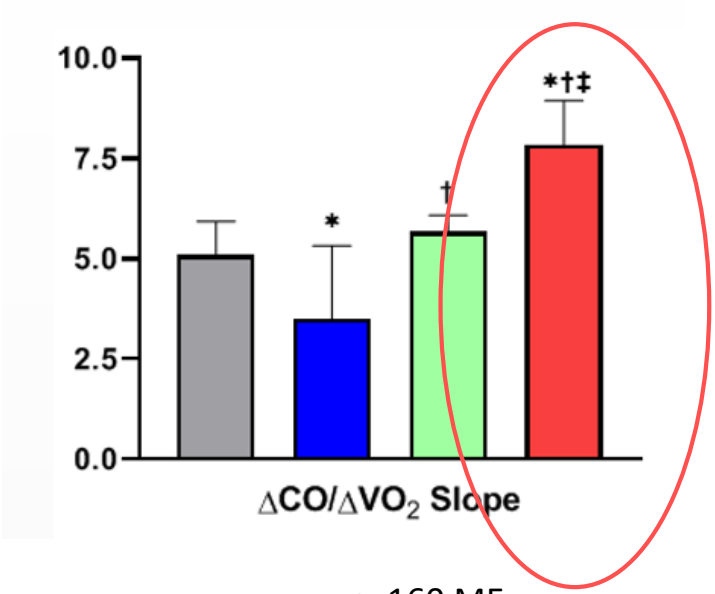
n=160 ME

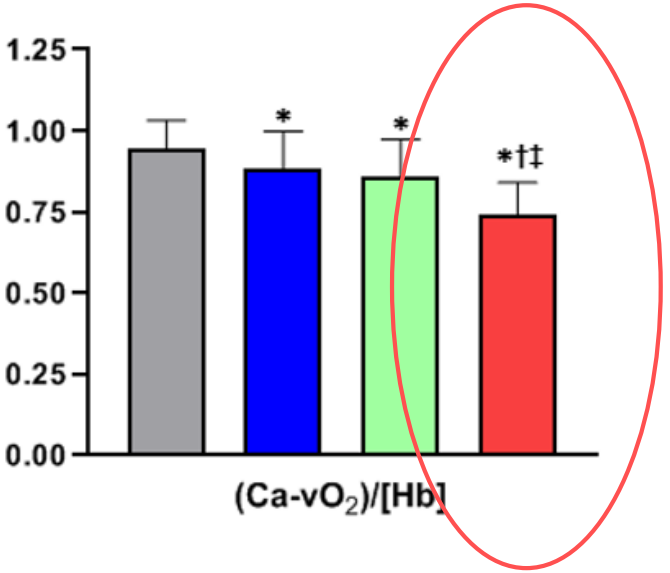


Chest. 2021 Aug;160(2):642-651. doi: 10.1016/j.chest.2021.01.082. Epub 2021 Feb 10. PMID: 33577778.

High flow = poor systemic 02 extraction

V02=Qc x (Ca-v02)





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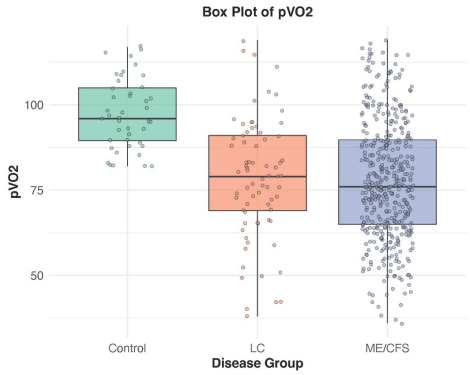
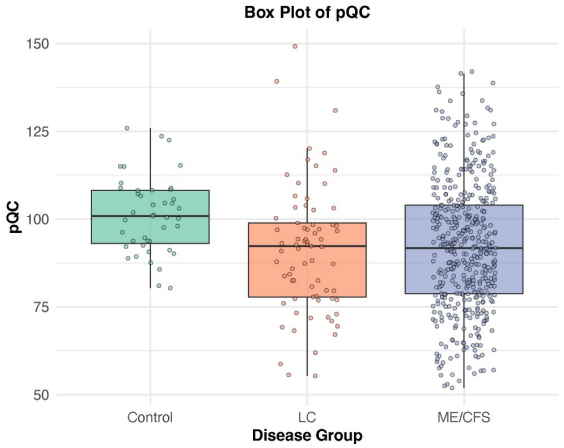
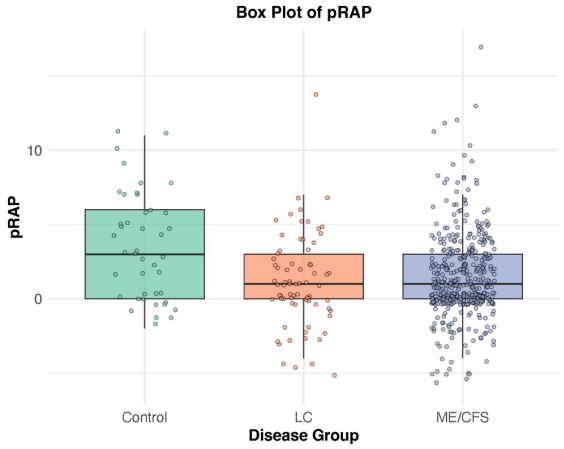
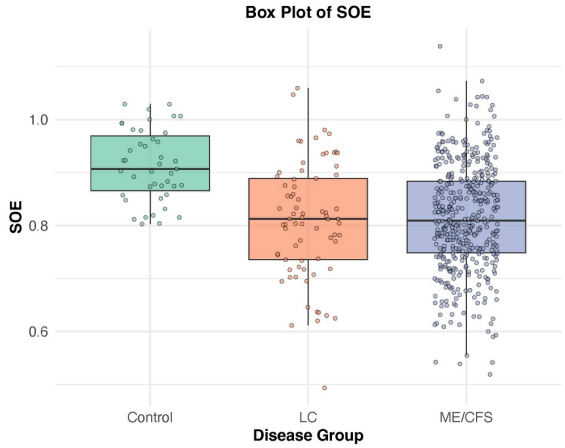
ME/CFS v. Long COVID v. Normal

n= 335 n=72 n= 43

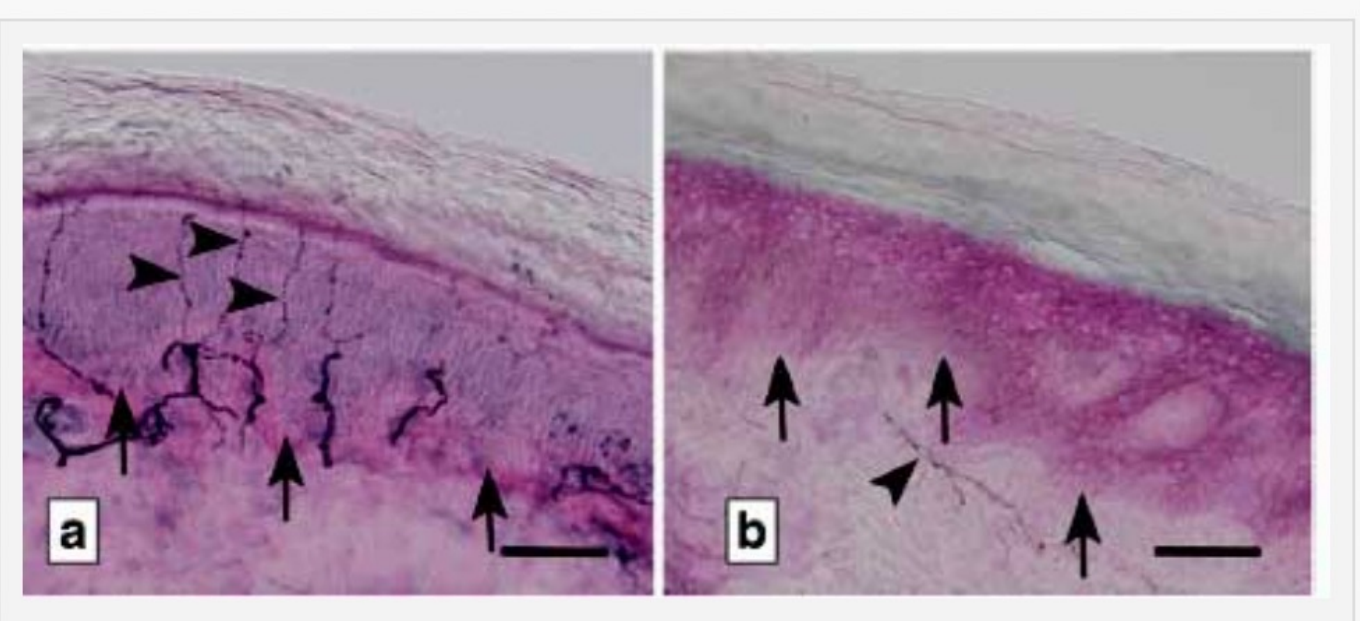






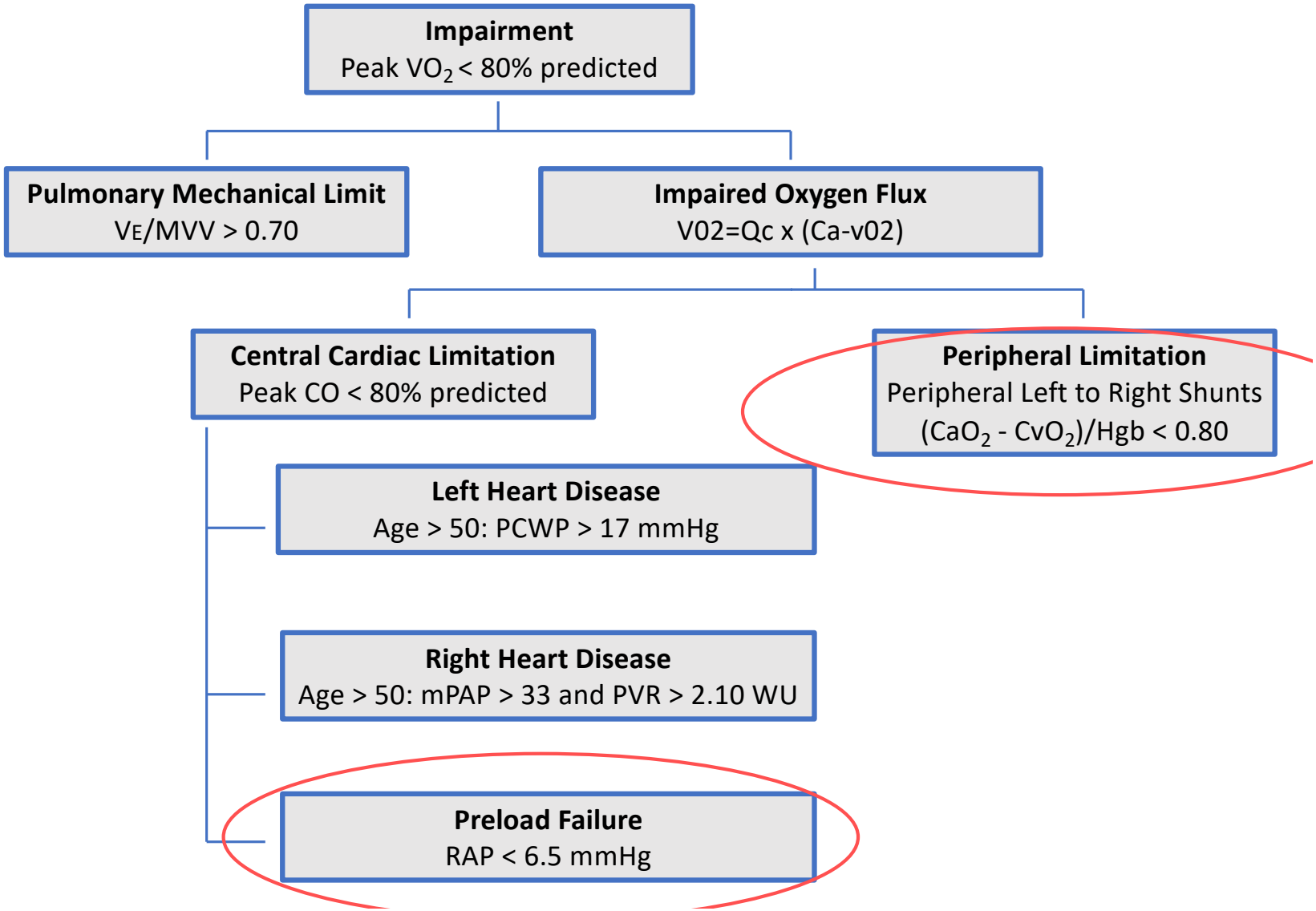


ME & LC
Small Fiber Neuropathy



- Group IV unmyelinated C fibers
- Skin bx Dx
- Pain/Dysautonomia
- 40+% in FM and POTS
- Assoc'd w/ AI and inflammation

n=407, 67%
Submitted, ERS 2025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> Chest. 2022 May 6;S0012-3692(22)00890-X. doi: 10.1016/j.chest.2022.04.146.
Online ahead of print.

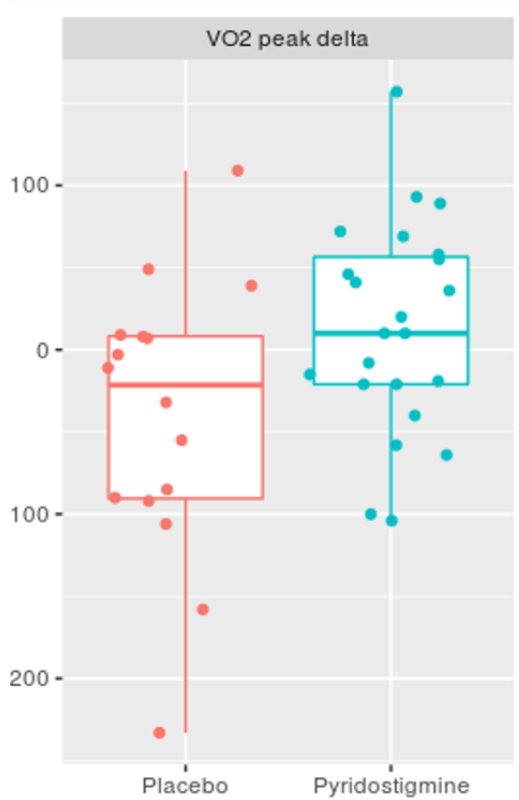
Neurovascular Dysregulation and Acute Exercise Intolerance in ME/CFS: A Randomized, Placebo-Controlled Trial of Pyridostigmine

Phillip Joseph [1], Rosa Pari [2], Sarah Miller [3], Arabella Warren [3], Mary Catherine Stovall [3], Johanna Squires [3], Chia-Jung Chang [4], Wenzhong Xiao [4], Aaron B Waxman [3], David M Systrom [5]

Affiliations + expand

PMID: 35526605 DOI: 10.1016/j.chest.2022.04.146

Pyridostigmine RCT: Peak Exercise V02



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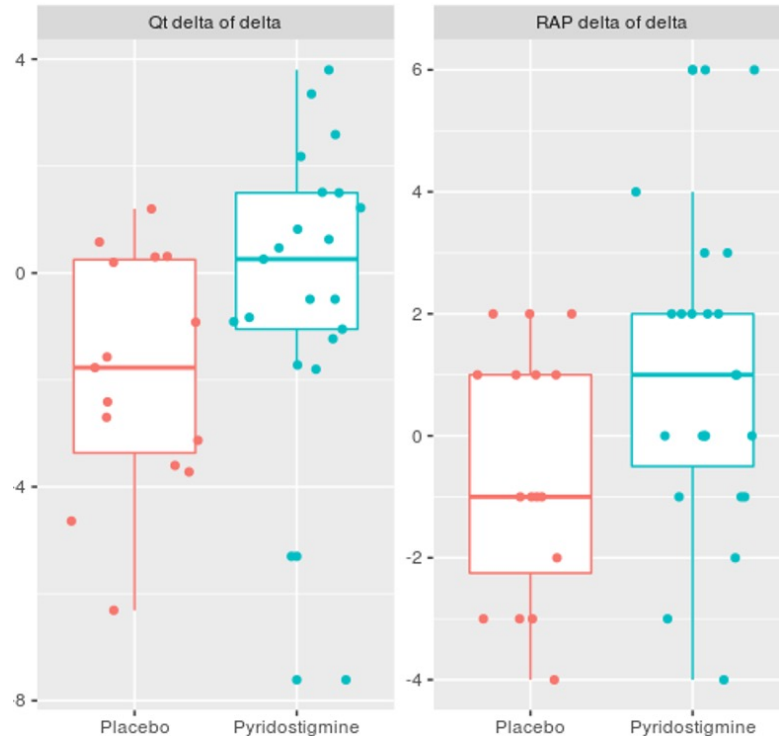
Pyridostigmine RCT:
Peak Exercise Cardiac Output and RAP



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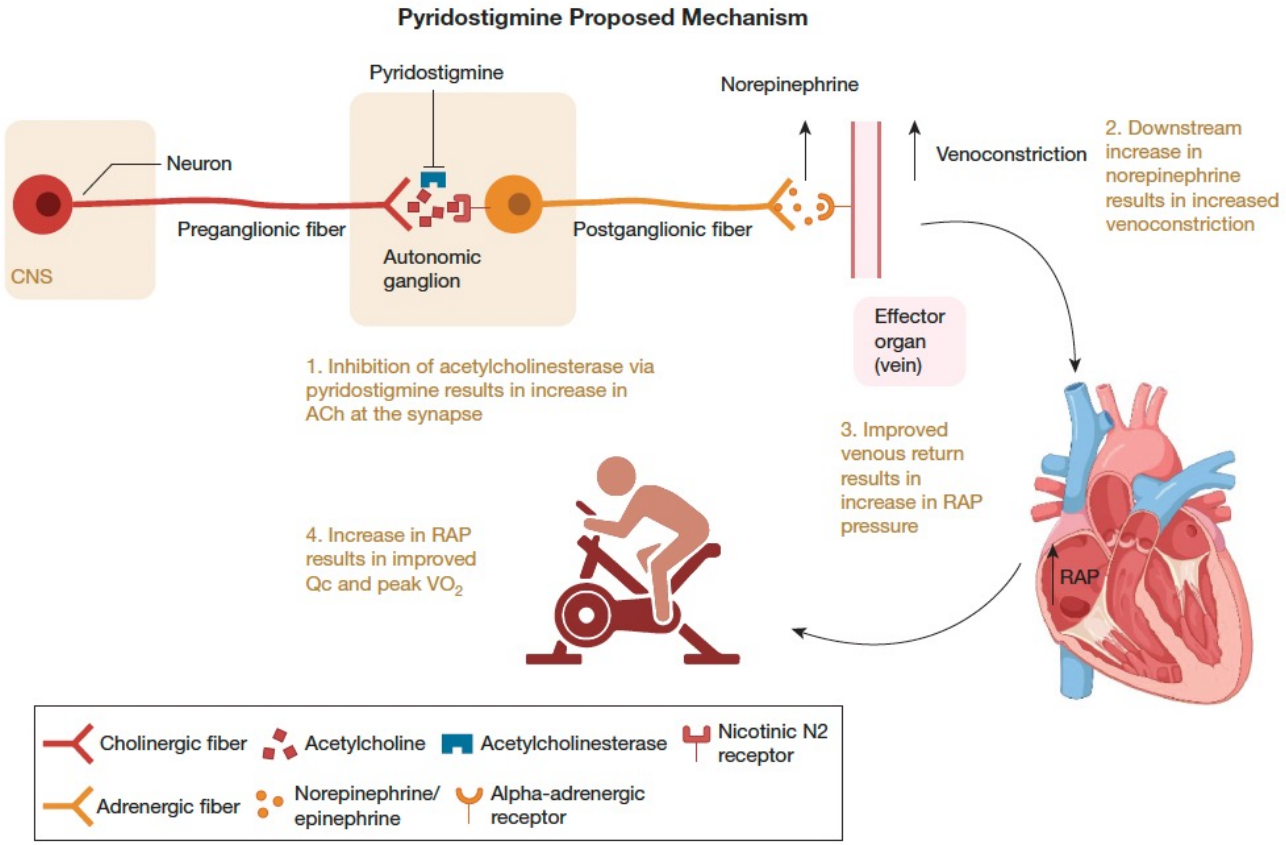
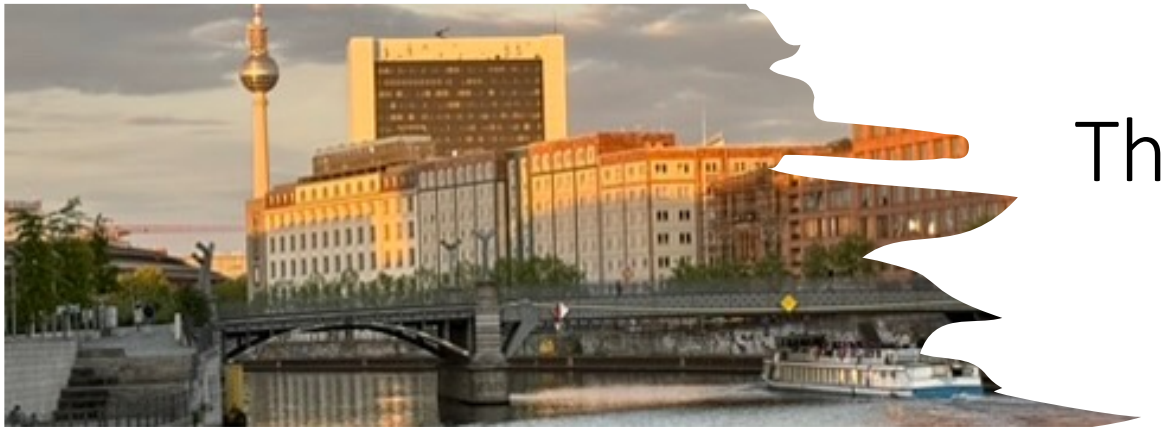
Pyridostigmine



Circulatory dysfunction in ME/CFS

- Systemic vascular dysregulation
  - Preload failure
  - Peripheral L to R shunting
- Small fiber neuropathy
  - Prevalent
- Corrects w/ pyridostgmine

>>>> Neurovascular dysregulation



Thank You!