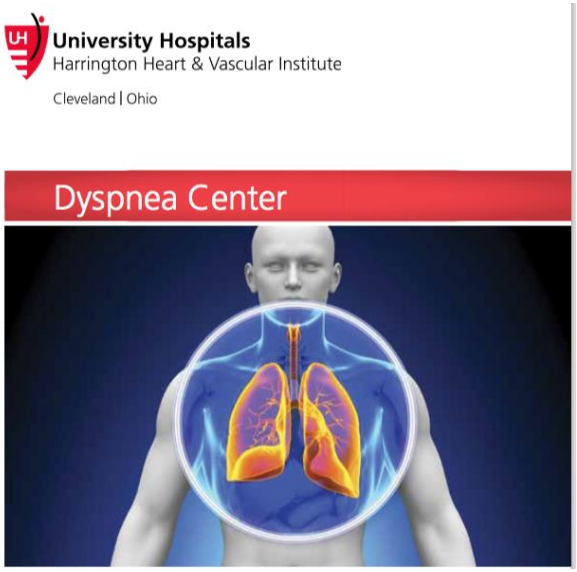
Lessons From An Advanced Dyspnea Center: New Approaches to An Old Problem



Robert Schilz DO, PhD

University Hospitals
Case Medical Center
Cleveland | Ohio

SCHOOL OF MEDICINE
CASE WESTERN RESERVE UNIVERSITY

Conflict of Interest Statement

- Robert Schilz DO, PhD
  - No conflicts relevant to this talk

Introduction, Definitions, Background

Objectives

- List current causes of "difficult to diagnose" chronic dyspnea
- Review standard evaluation of the dyspneic patient
- Discuss advanced imaging, exercise and cardiopulmonary testing available

Variable Definitions Of Dyspnea

- Unpleasant or uncomfortable respiratory sensations
- Difficult, labored, uncomfortable breathing
- Awareness of respiratory distress
- The sensation of feeling breathless or air hunger
- An uncomfortable sensation of breathing

- ATS guidelines: subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity

ATS. AJRCCM, 1999.

Dyspnea Symptom Prevalence

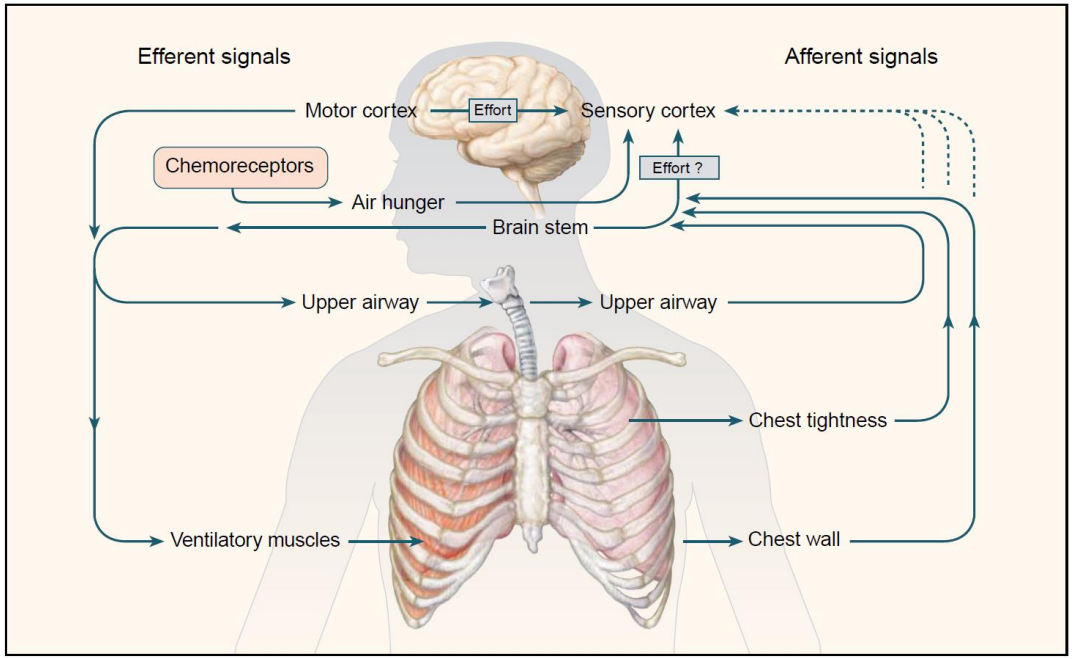
- Epidemiology of the problem:
  - 9-13% community residing adults have mild-moderate dyspnea
  - Age 40 or over: 15 – 18%
  - Age 70 or over: 25 – 37%

- Responsible for 3 – 4 million yearly ED visits

Parshall, AJRCCM 2012:185;435

Mechanisms Of Dyspnea: Respiratory Center Output

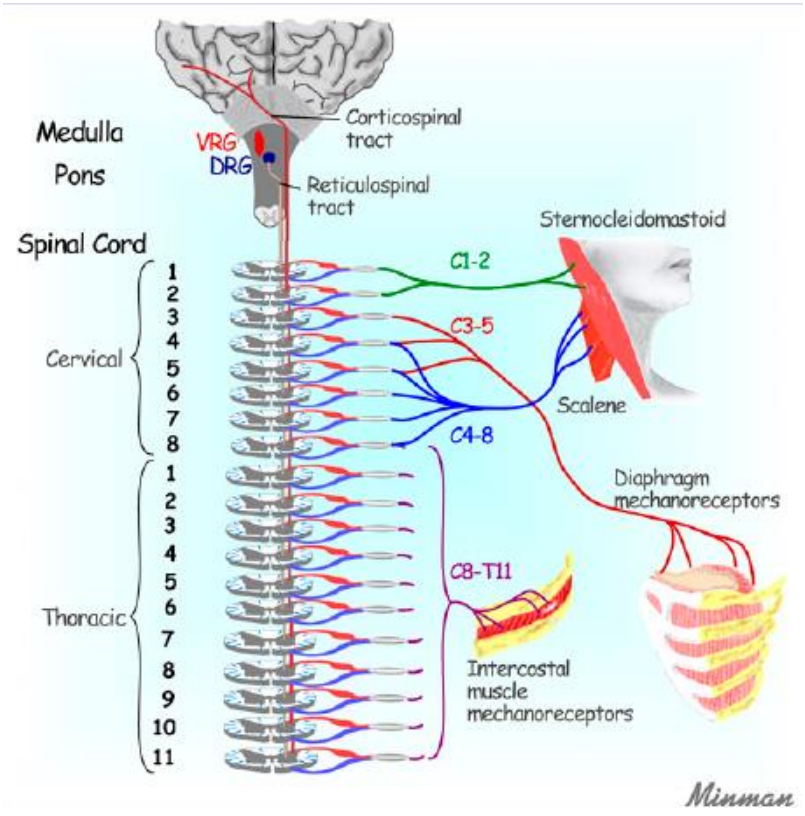
- Chemoreceptors
  - Peripheral: carotid bodies, aortic arch
    - Sense changes in PO2, acidosis, hypercapnea
  - Central: medulla
    - pH and PCO2 changes
- Hypercapnea
  - Potent stimulus of dyspnea
- Hypoxia
  - Less potent stimulus than hypercapnea



Manning. NEJM, 1995.

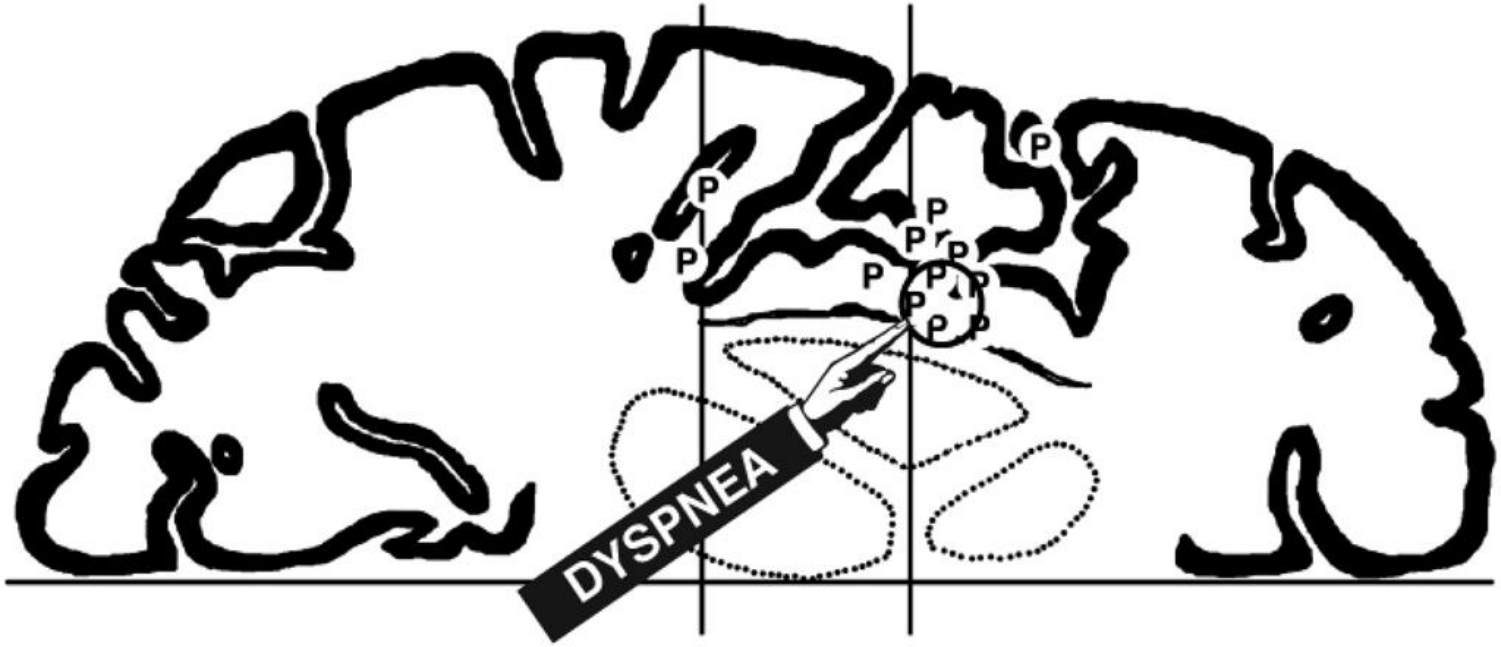
Mechanisms Of Dyspnea: Stimulation Of Mechanoreceptors

- Mechanoreceptors
  - Upper airway
  - Pulmonary receptors
    - Limitations of movement exacerbate dyspnea
    - The sensation of dyspnea varies with activation
  - Chest wall receptors
    - Restricted motion exacerbates dyspnea
    - Redundant to pulmonary receptors



Nausherwan. Chest, 2010.

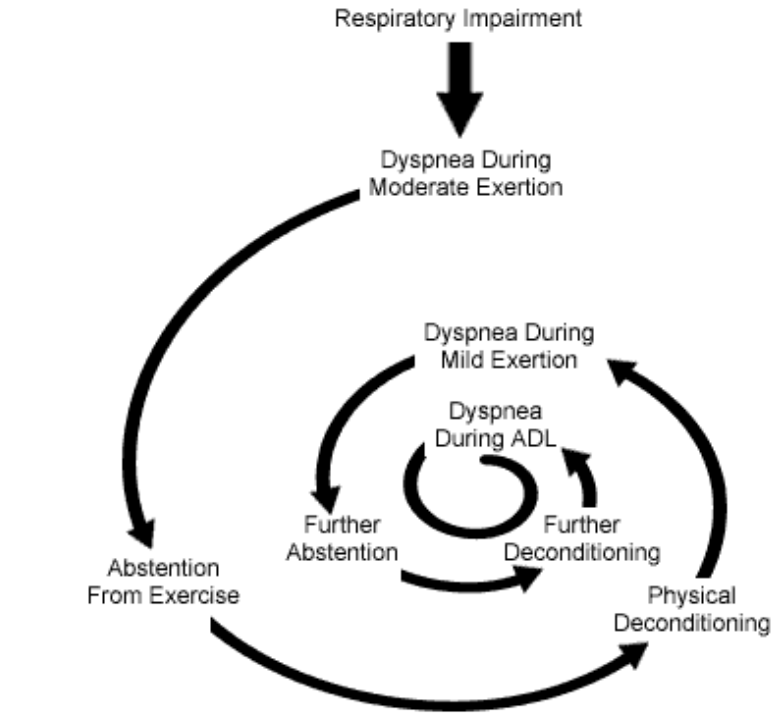
Neuropsychological Components of Dyspnea



Pain and Dyspnea in the **Anterior Insula.** One of the key brain regions activated in both dyspnea and pain is the anterior insula. The “P” symbols show the locations of pain activations of the insula in a transverse slice at Z=+8. Pain data from various studies summarized by a meta analysis (Peyron et al. 2000). The larger circle labeled “D” shows the area activated by dyspnea (Banzett et al. 2000).

Lansing, Respir Physiol Neurobiol. 2009:167(1);53-60

The Dyspnea Spiral



ADL = activities of daily living

from Haas F, Salazar-Schicchi J, Axen K. Desensitization to dyspnea in chronic obstructive pulmonary disease. In: Casaburi R, Petty TL, eds. Principles and Practice of Pulmonary Rehabilitation. Philadelphia, PA, WB Saunders Company;1993:241-25.

Exercise Training Decreases Dyspnea and the Distress and Anxiety Associated With It*

Monitoring Alone May Be as Effective as Coaching

Virginia Carrieri-Kohlman, DNSc, RN; Jenny M. Gormley, MSN, RN; Marilyn K. Douglas, DNSc, RN; Steven M. Paul, PhD; and Michael S. Stulbarg, MD

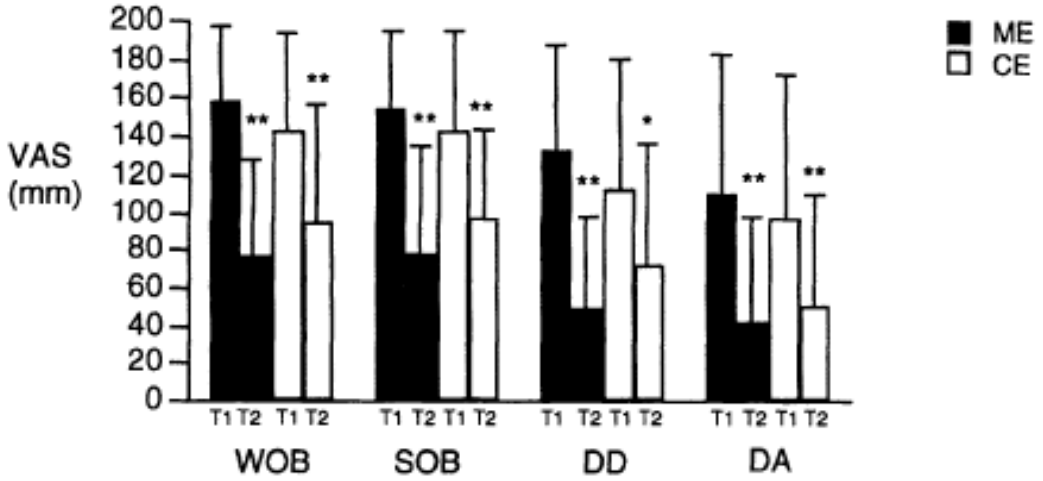
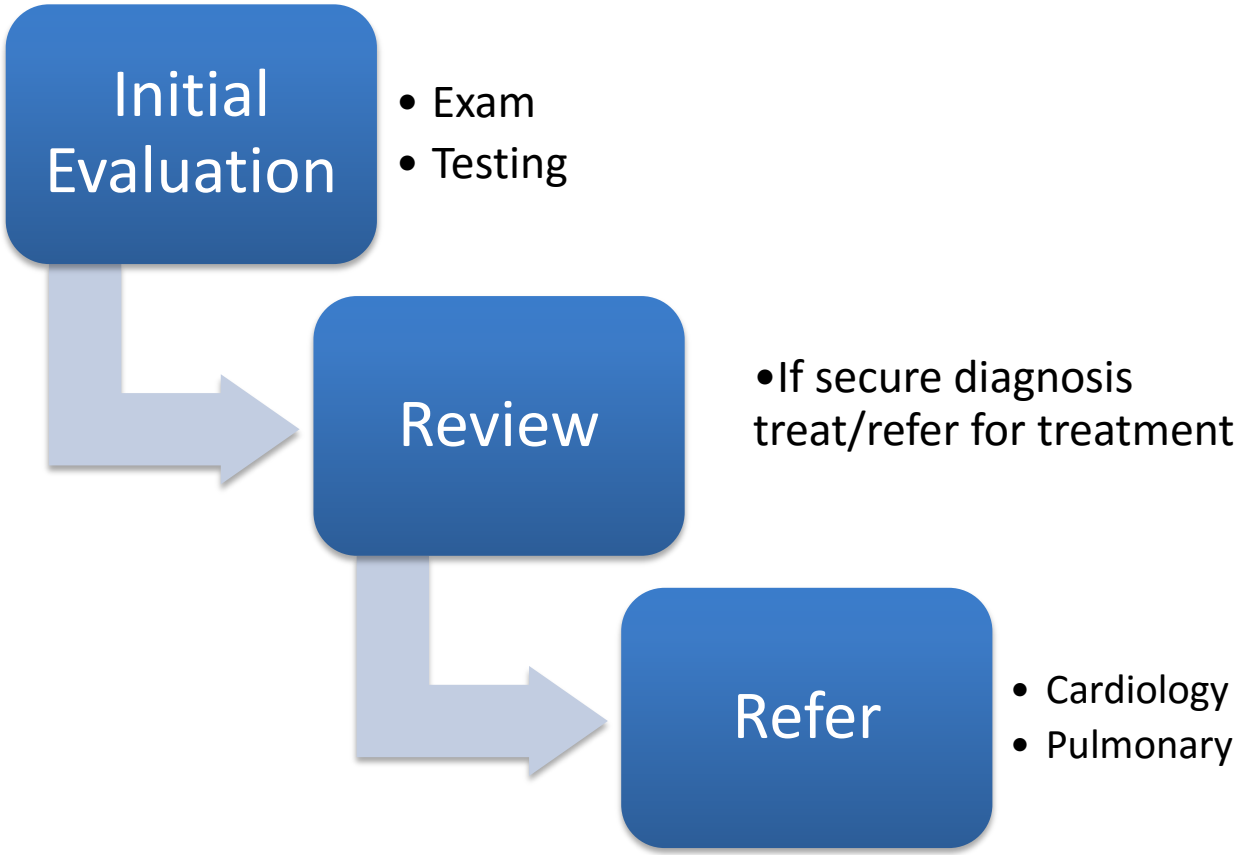


FIGURE 2. Dyspnea components at isostage during treadmill ST at T1 and T2 for ME (n=27) and CE (n=24) groups. Isostage was the same stage during ST at T2 as that of the maximum stage achieved during ST at T1. Asterisk indicates $p<0.01$; two asterisks, $p<0.001$.

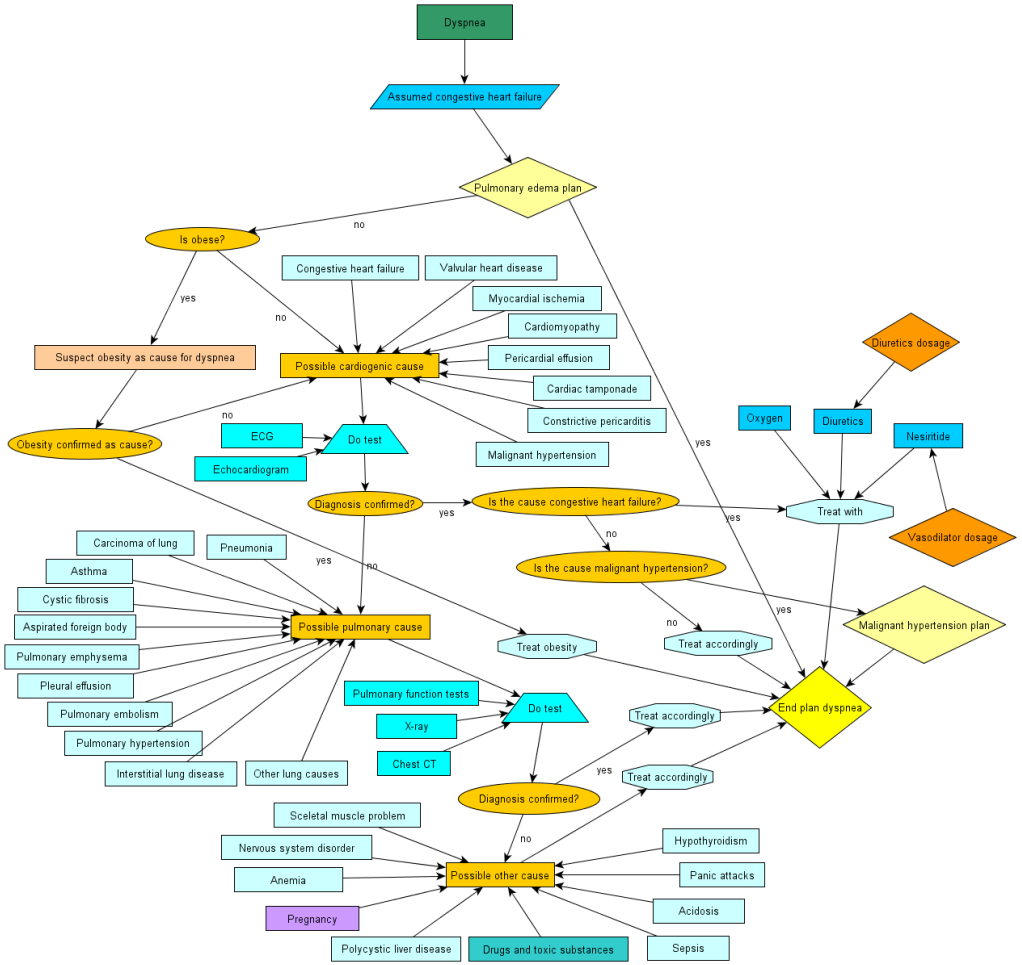
Carrieri-Kohlman, Chest. 1996:110;1526-1535

Traditional Approach to the Patient with Chronic Dyspnea

Typical Stepwise Evaluation in Dyspnea

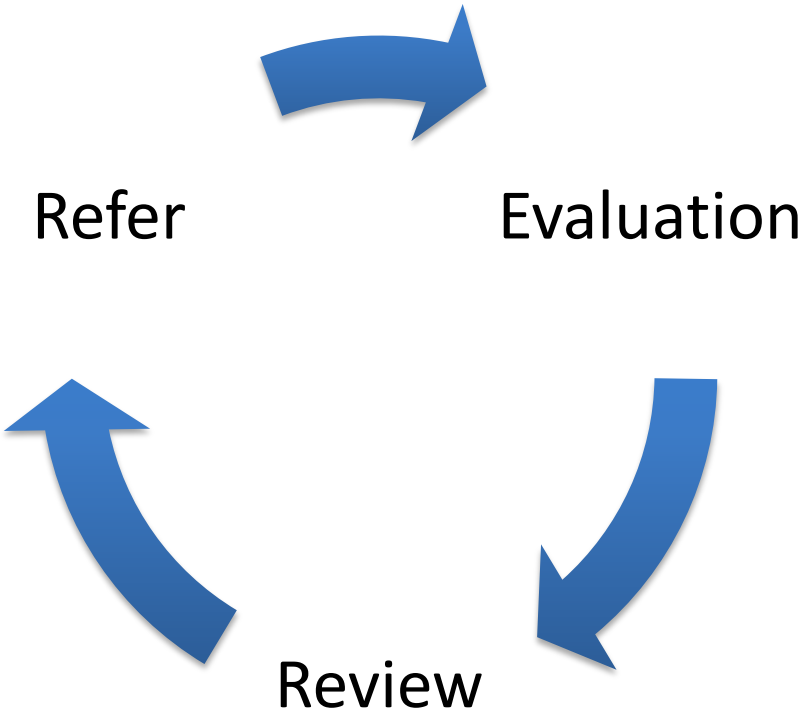


Typical Dyspnea Evaluation and Differential Diagnosis



Typical Argument Among Consultants: Is It The Heart or the Lungs?

Typical Outcome of the Process



Differential Diagnosis of Chronic Dyspnea

- Cardiac
  - Heart failure
  - Coronary artery disease
  - Arrhythmia
  - Pericardial disease
  - Valvular heart disease
- Pulmonary
  - Chronic obstructive pulmonary disease
  - Asthma
  - Interstitial lung disease
  - Pleural effusion
  - Pulmonary hypertension
  - Malignancy
  - Bronchiectasis
- Non-cardiac/Non-pulmonary
  - Thromboembolic disease
  - Psychogenic
  - Deconditioning
  - Obesity
  - Anemia
  - GERD
  - Metabolic conditions
  - Cirrhosis
  - Thyroid disease
  - Neuromuscular
  - Chest wall
  - Upper airway
  - Medications

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  - Neuromuscular
  - Chest wall
  - Upper airway
  - Medications

Differential Diagnosis of Chronic Dyspnea

Cardiac	Pulmonary	Peripheral
Coronary Ischemia	Obstructive lung dz (COPD, asthma, chronic bronchitis)	Mitochondrial myopathy
Cardiomyopathy	Interstitial lung dz	Muscular dystrophy
Atrial Fibrillation	Lung cancer	Phrenic nerve palsy
Valvular Heart Disease (AS,MR,MS)	Pulmonary HTN	Anemia, acidemia, hyperthyroidism
Congenital Heart Dz	Chest wall deformity, upper airway dysfunction , vocal cord dysfunction	Obesity, deconditioning

Table 2 – Step approach to the evaluation of unexplained dyspnea

Step 1 – Initial assessment
History and physical examination
Chest radiography
Spirometry
Pulse oximetry

Step 2 – Focused testing
Bronchoprovocation challenge testing
Electrocardiography
Further pulmonary function testing in older persons and high-risk groups
Laboratory tests: hemoglobin measurement, thyroid function tests, and renal panel in high-risk groups
Laryngoscopy if clinical history or flow-volume loop suggests vocal cord dysfunction
CT and/or bronchoscopy if chest radiograph is abnormal

Step 3 – Cardiopulmonary exercise testing (CPET)
Determine the exercise response pattern

Step 4 – Specialized tests (or additional steps) based on CPET results
Normal
- Reassurance
- Gastroesophageal reflux evaluation and treatment
- Psychiatric evaluation

Hyperventilation/psychogenic
- Behavioral therapy
- Psychiatric evaluation and treatment

Obesity
- Weight loss and exercise training program

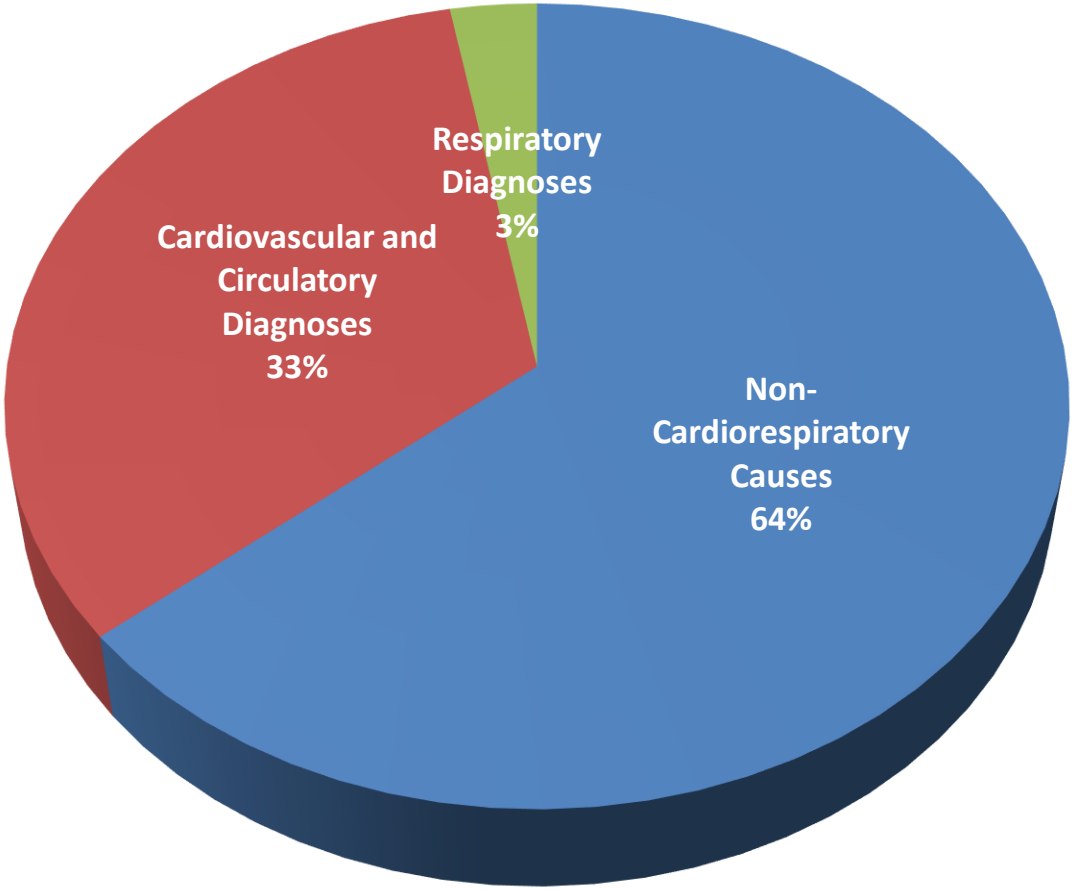
Cardiac/ischemia
- Cardiac functional assessment
- Cardiac catheterization
- Cardiac pattern with gas exchange abnormalities: evaluation for pulmonary vascular disease if gas exchange abnormalities are present

Cardiac/deconditioning
- Echocardiography, cardiac functional assessment
- Exercise training program
- Muscle biopsy

Pulmonary
- Obstructive lung disease: treatment
- Interstitial lung disease: high-resolution CT, lung biopsy

Adapted from Niven AS, Weisman IM. In: Mahler DA, O'Donnell DE, eds. *Dyspnea: Mechanisms, Measurement, and Management.* 2nd ed. 2005.[10]

Causes of Dyspnea in a Pulmonary Clinic

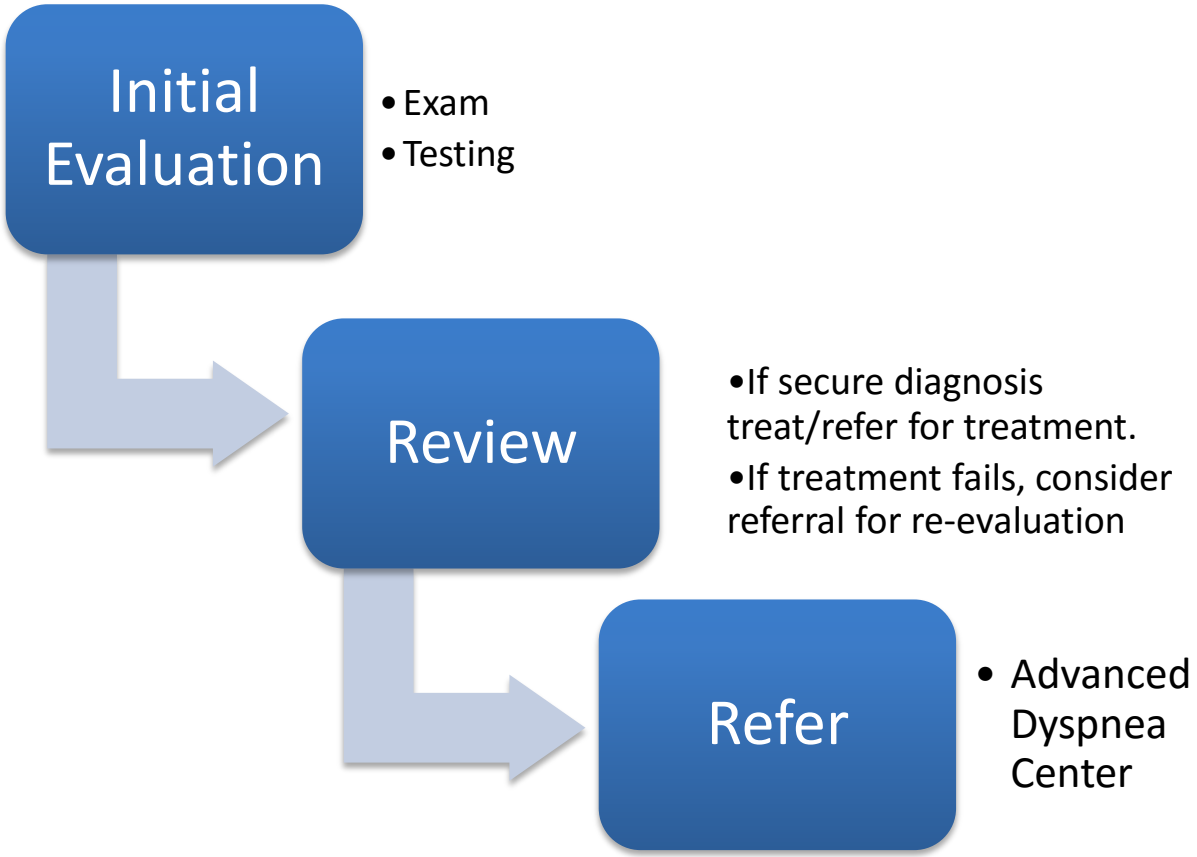


Pratter et al. Respiratory Medicine Volume 105, Issue 7, Pages 1014–1021

Problems with this Approach

- No accounting for layers of referral
- No accounting for difficulties in some diagnoses
  - HFPEF
  - Pulmonary Arterial Hypertension
  - Vocal Cord Dysfunction
- No accounting for diversions of diagnoses due to comorbidities

Alternate Practical Approach to the Evaluation of Dyspnea



Initial Evaluation of Chronic Cryptogenic Dyspnea

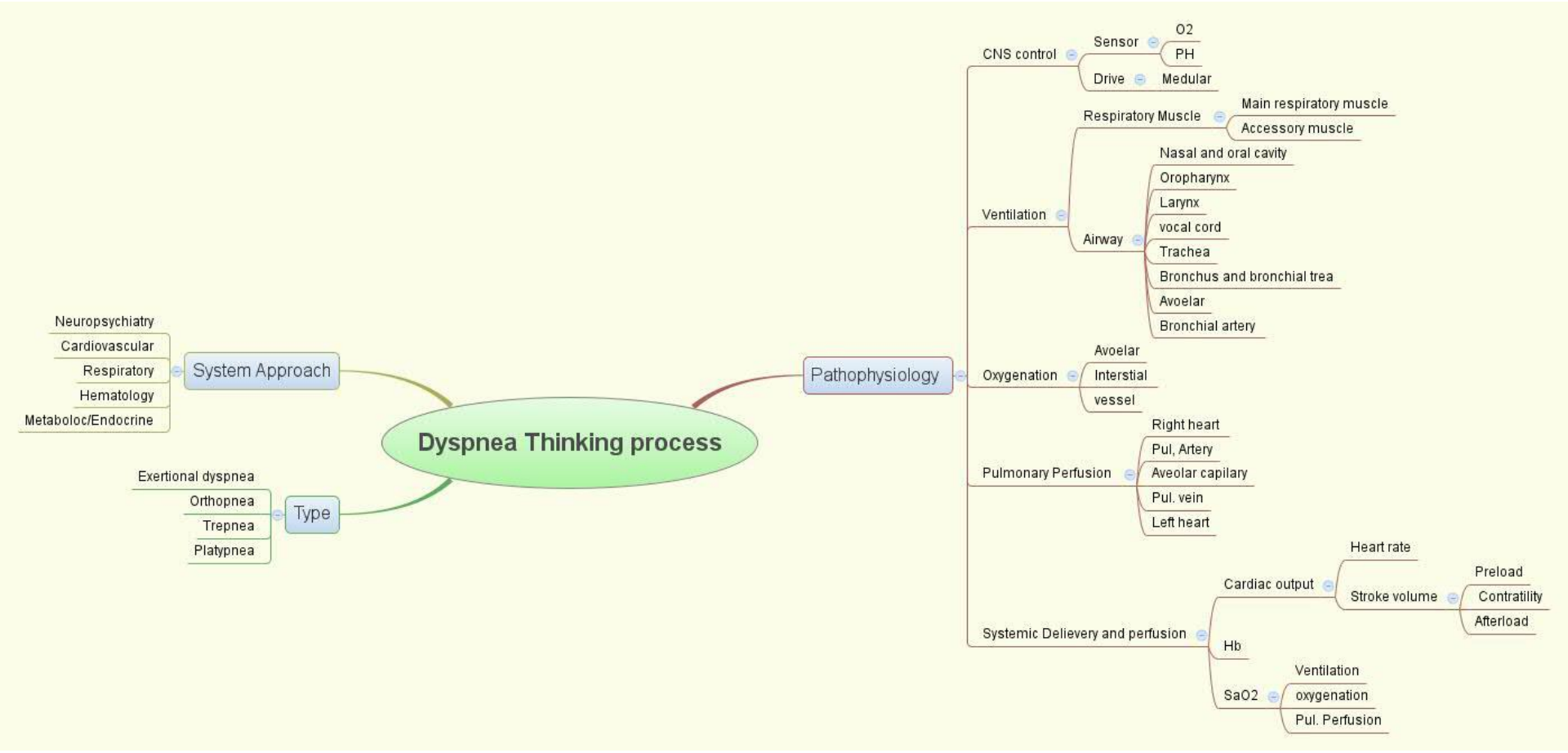
- Level I
  - History and Physical Exam
  - Pulse Oximetry, Spirometry
  - Chest Radiography
- Level II
  - EKG
  - Lab: CBC, Thyroid Function, Electrolytes and Hepatic and Renal Function
  - CT Scanning
- Level IV
  - Echocardiography

Initial Evaluation of Chronic Cryptogenic Dypsnea

- Level I
  - History and Physical Exam
  - Pulse Oximetry, Spirometry
  - Chest Radiography
- Level II
  - EKG
  - Lab: CBC, Thyroid Function, Electrolytes and Hepatic and Renal Function
  - CT Scanning
- Level IV
  - Echocardiography

Caveat: Tests are performed at rest!

Dyspnea Center Approach to the Patient with Chronic Dyspnea



Pathophysiology for the Health Professions by Barbara E Gould

Our Approach To The Patient with Chronic Cryptogenic Dyspnea – Initial Testing and Review

- History and physical
- EKG
- Echocardiogram
- CXR/CT scan
- Spirometry, pulse oximetry rest and ambulatory
- Cardiopulmonary exercise testing

Consider Advanced Non-Invasive/Minimally Invasive Studies in Dyspnea Evaluation

- Complete PFTs (Dco, Lung volumes, Flow-volume loops, Resp. pressures, ABG)
  - During exercise
  - Methacholine testing
  - Positional
- Airway inspection +/- Exercise
  - Endoscopic
  - Dynamic CT
- Echocardiogram
  - Exercise
  - Bubble studies

Consider Invasive Procedures in Dyspnea Evaluation

- Cardiac Catheterization
  - RHC
    - Volume Loading
    - Nitroprusside
    - NO Challenge
    - Simple Exercise
  - LHC
  - iCPET
- Muscle Biopsy
- Open Lung Biopsy

Why evaluate with exercise?

- "Dyspnea is a complex symptom that potentially warns of a critical threat to homeostasis and thus frequently leads to adaptive responses (such as rest)".[1]

- Exercise is the ideal stimulus to interrogate the cardiovascular system
  - Increases oxygen consumption and minute ventilation by 3 – 15x baseline utilization
  - Improves signal to noise ratio of test

- Most patients are not dyspneic at rest. Why not test them when they have symptoms?

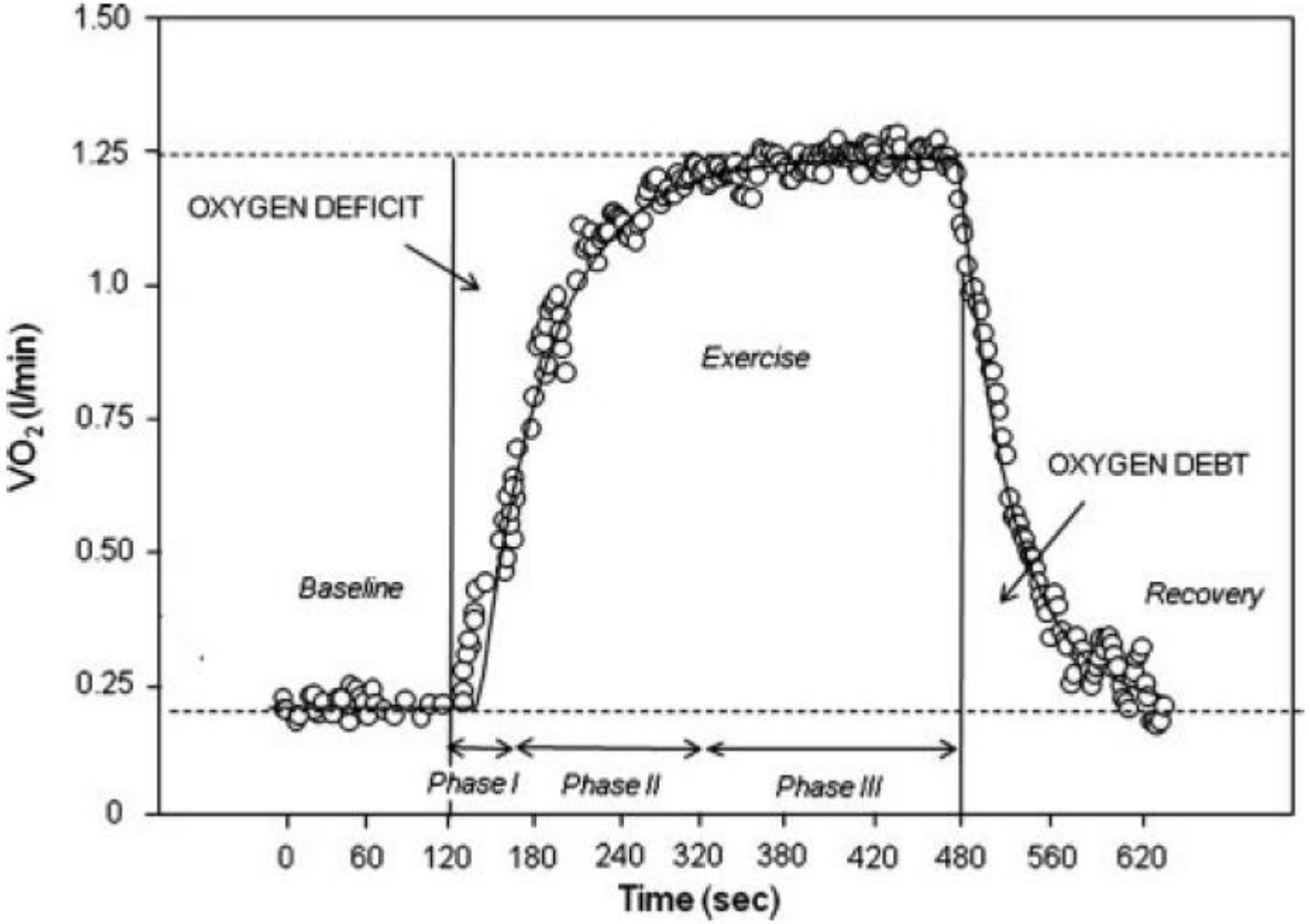
[1]Parshall, AJRCCM 2012:185;435

Non-Invasive Cardiopulmonary Exercise Testing

Cardiopulmonary Exercise Test (CPET)

http://www.medgraphics.com/download/UltimaCardiO2_4pg_060105-001rA.pdf

Exercise is the ideal stimulus



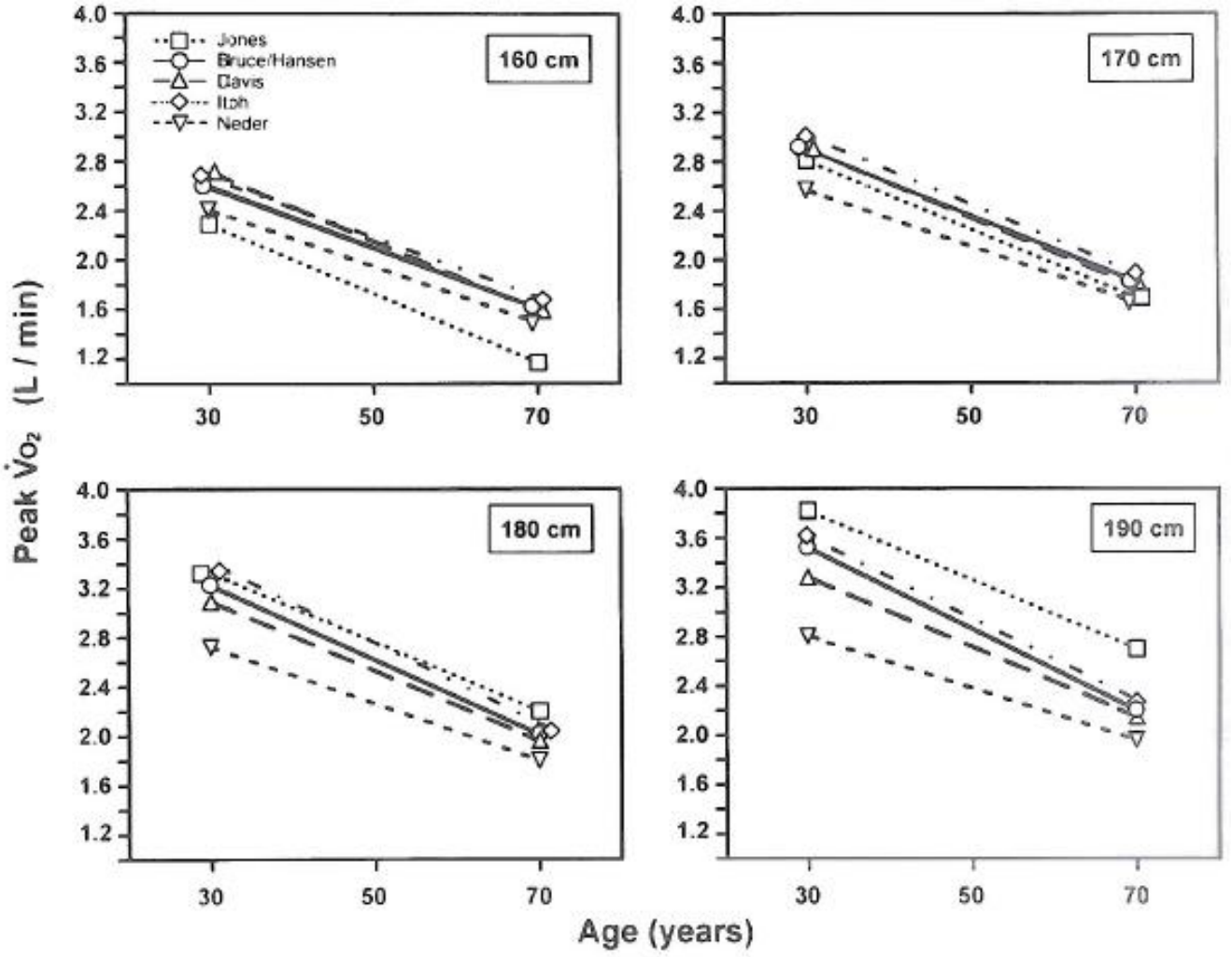
Balady, Circ 2010:122;191

Common Variables Measured

Variable	Definition	Clincial Signficance
VO_2 Peak (O_2 ml/kg/min)	Highest demonstrable VO_2	Expression of aerobic exercise capacity
VT (O_2 ml/kg/min)	VO_2 at which there is an accelerated rise in VE & VCO_2 relative to VO_2	Measure of fitness (usually about 50-65% of VO_2 Max)
RER (VCO_2 / VO_2)	Ratio at max exercise	Indicator of subject effort (RER >1.10)
VE / VCO_2 (Ventilatory efficiency) (VE = minute ventilation)	Efficiency of pulmonary clearance of CO2 during exercise	Reflects V/Q matching (can be used for severity index)
Breathing reserve	Relation of max VE and pre-test max voluntary ventilation (MVV)	Index of physiologic reserve of lung (low in COPD and trained athletes)
Oxygen Pulse (VO_2/HR)	Ratio of oxygen consumption to HR	Surrogate Marker for Stroke Volume

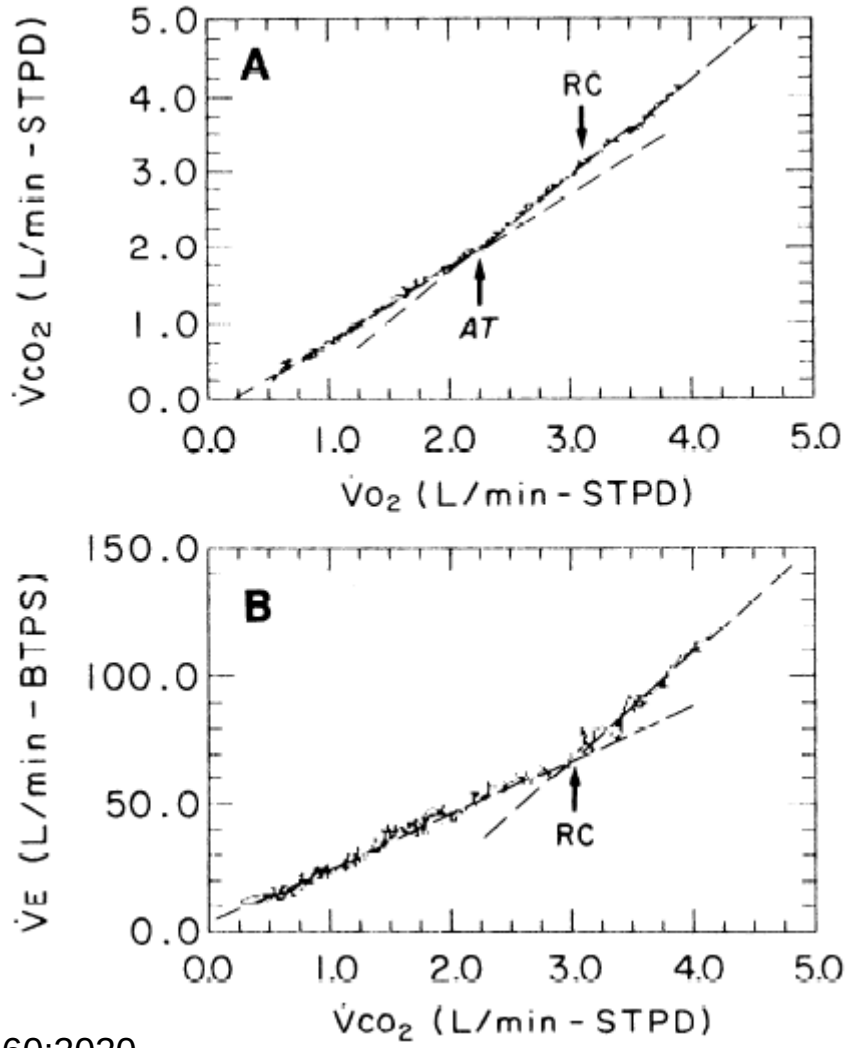
Modified from: Siestema Circ. 2011;123:668-680

VO_2 Peak Declines with Age



Wasserman Principles of Exercise Testing & Interpretation 3rd Ed. 1999: p. 145

Determination of Anaerobic Threshold (Beaver & Wasserman)



Beaver J Appl Physiol 1986:60;2020

Ventilatory Efficiency (VE/VCO_2)

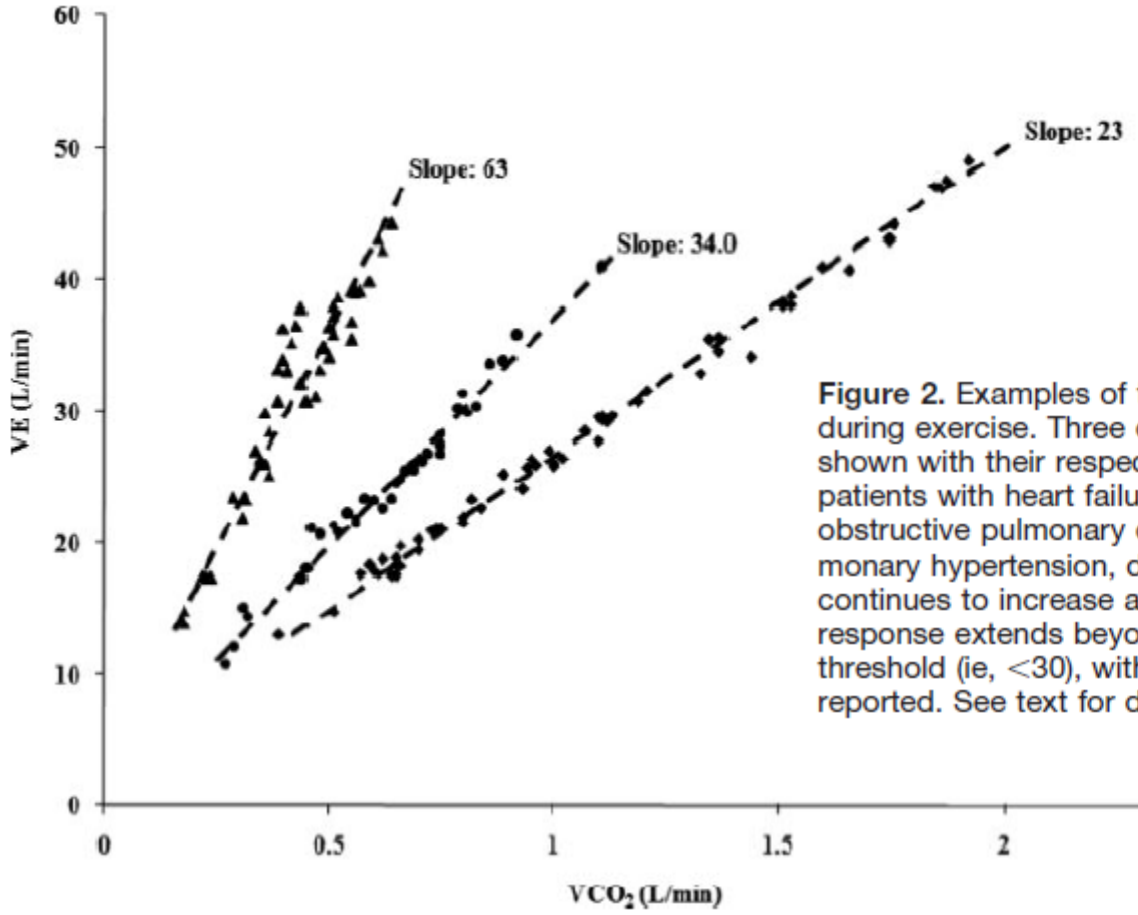


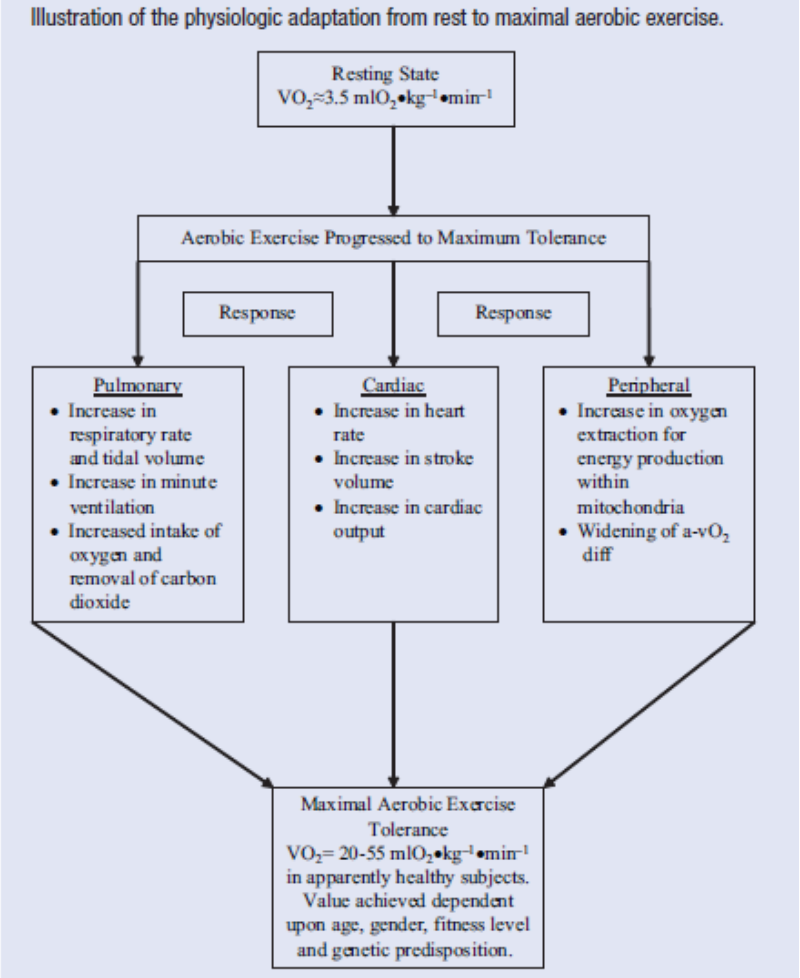
Figure 2. Examples of the $\dot{V}E/\dot{V}CO_2$ slope during exercise. Three different slopes are shown with their respective values. In patients with heart failure, chronic obstructive pulmonary disease, and pulmonary hypertension, disease severity continues to increase as $\dot{V}E/\dot{V}CO_2$ response extends beyond the normal threshold (ie, <30), with values >60 being reported. See text for details.

Balady, Circ. 2010;122:191-225

Variables on CPET that suggest cardiac vs pulmonary exercise limitation

Findings to suggest cardiac cause	Findings to suggest pulmonary cause
Low “oxygen pulse” (VO2/HR) a surrogate of stroke volume	Reduced breathing reserve (< 15%)
ECG changes indicative of ischemia	Arterial desaturation (pulse oximetry)
Blunted or decreased HR or BP response to exercise	Elevated VE/VCO2 ratio

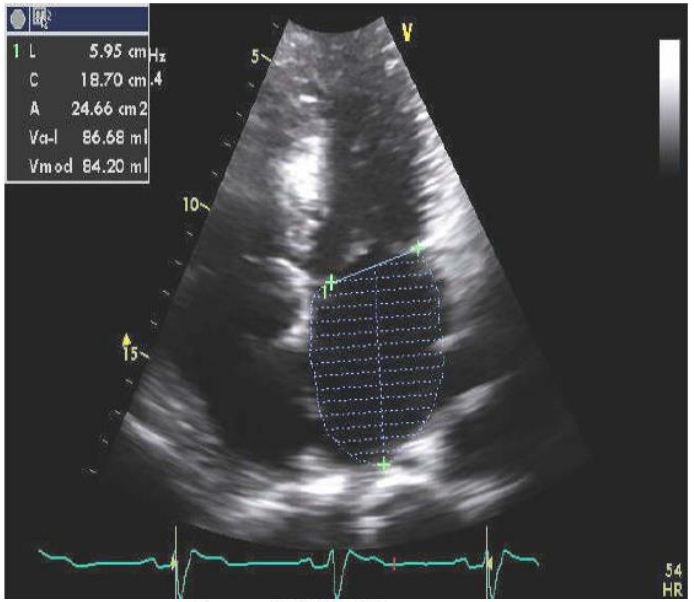
Diagnostic Patterns of Abnormal CPET Results

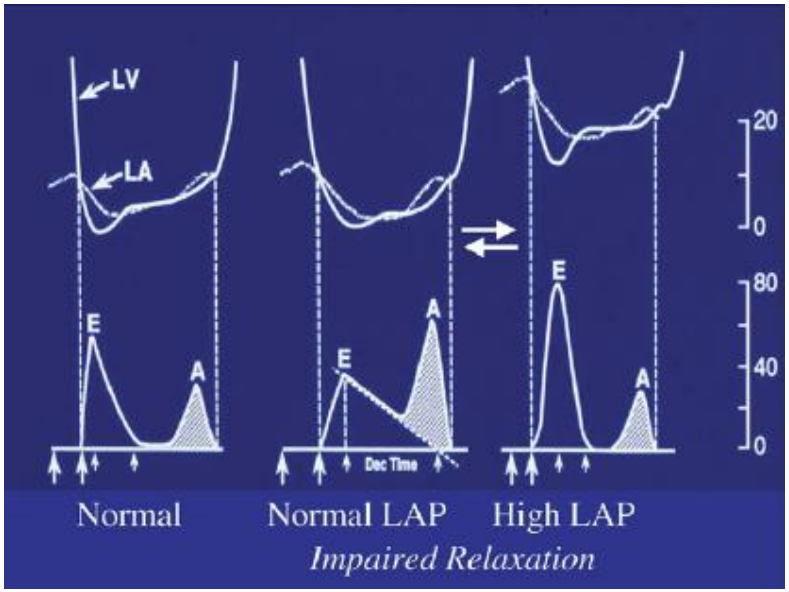


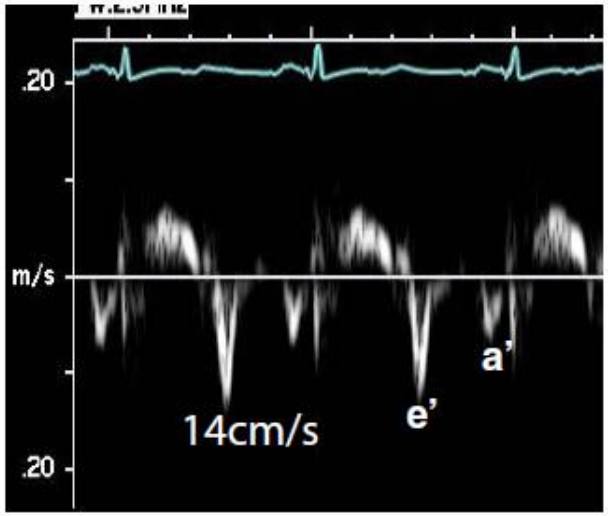
Arena Am J Lifestyle Med 2008

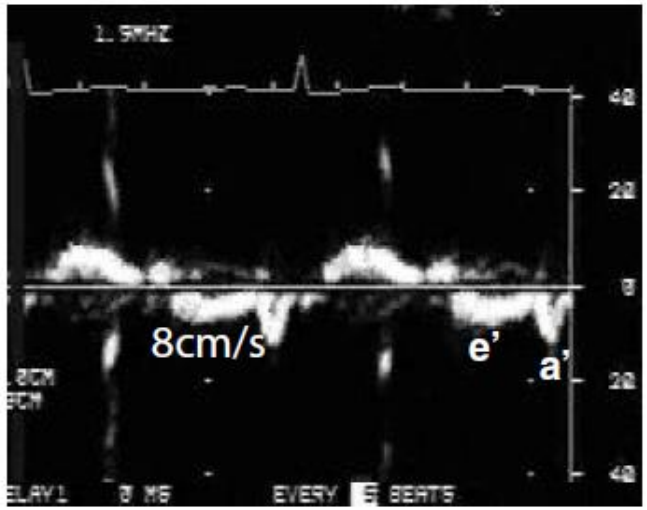
Exercise Echo Testing

What Does DHF Look Like On Echo?









Nagueh. JASE, 2009.

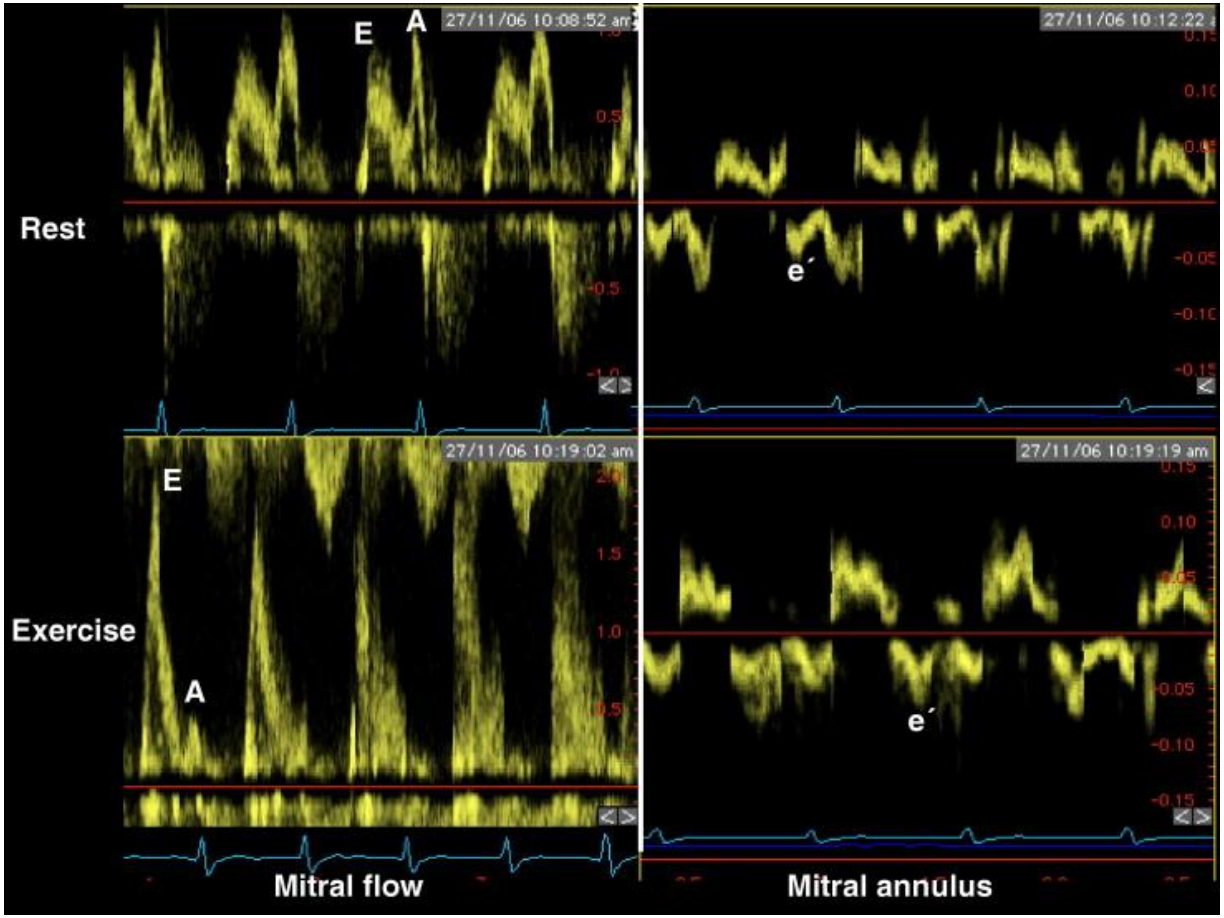
Normal
35 years old

Hypertension with LVH
58 years old

Diastolic Stress Echo

E/e’ 17

E/e’ 24



Peteiro, JASE 2008;21:178

Pulmonary Hypertension Stress Echo

Rest 4 Chamber View

Peak Exercise 4 Chamber View

Additional Exercise Echo Studies

- Assess wall motion abnormalities
- Assess valvular gradients and function with exercise
- Check bubble study to assess PFO shunting during exercise with hypoxic patients with minimal shunt during rest

Invasive Cardiopulmonary Exercise Testing

UH iCPET

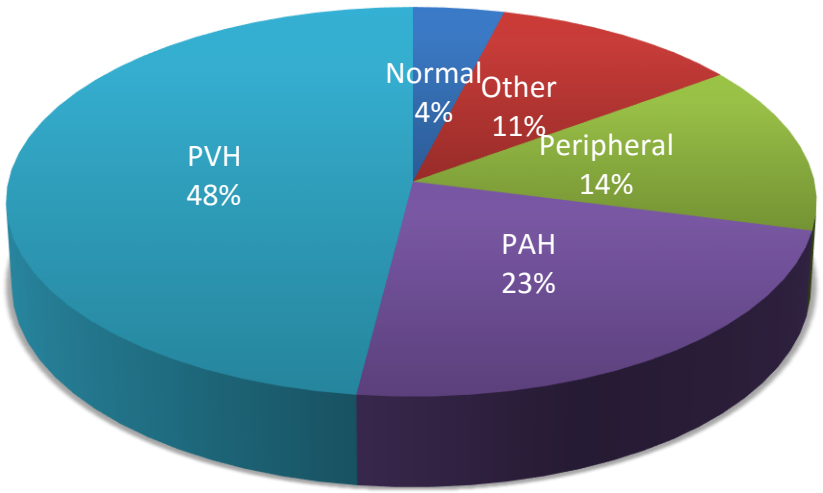
I-CPET Allows for Hemodynamic Phenotyping

- Peak Exercise mean PAP and LAP (via PCWP)
- Peak Exercise mixed venous O2 saturation
- Δ CaO_2 – CvO_2 gradient
- Fick Cardiac Output
- Pulmonary Vascular Resistance: PVR = (mPAP – LAP)/CO
- Δ mPAP (mm Hg) / Δ Cardiac Output (L/min)

Exercise-Induced Pulmonary Arterial Hypertension

James J. Tolle, MD; Aaron B. Waxman, MD, PhD; Teresa L. Van Horn, BA;
Paul P. Pappagianopoulos, MEd; David M. Systrom, MD

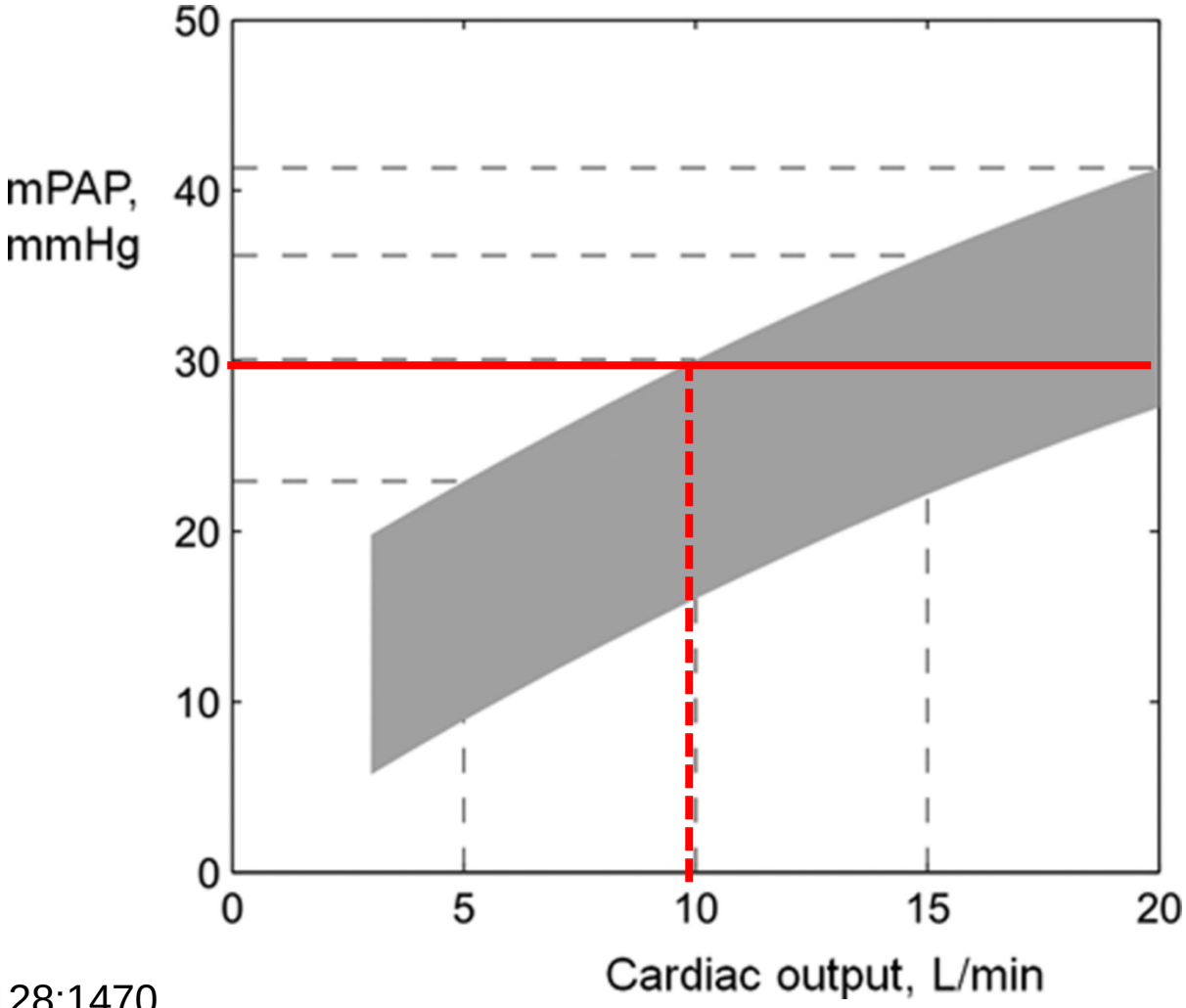
CPET Diagnoses



- The MGH CPET lab performed 406 studies over 3 year period
- Each patient had RHC, A-line placed and CO calculated by first pass radionuclide ventriculography
- 75% of studies performed to evaluate dyspnea of uncertain etiology

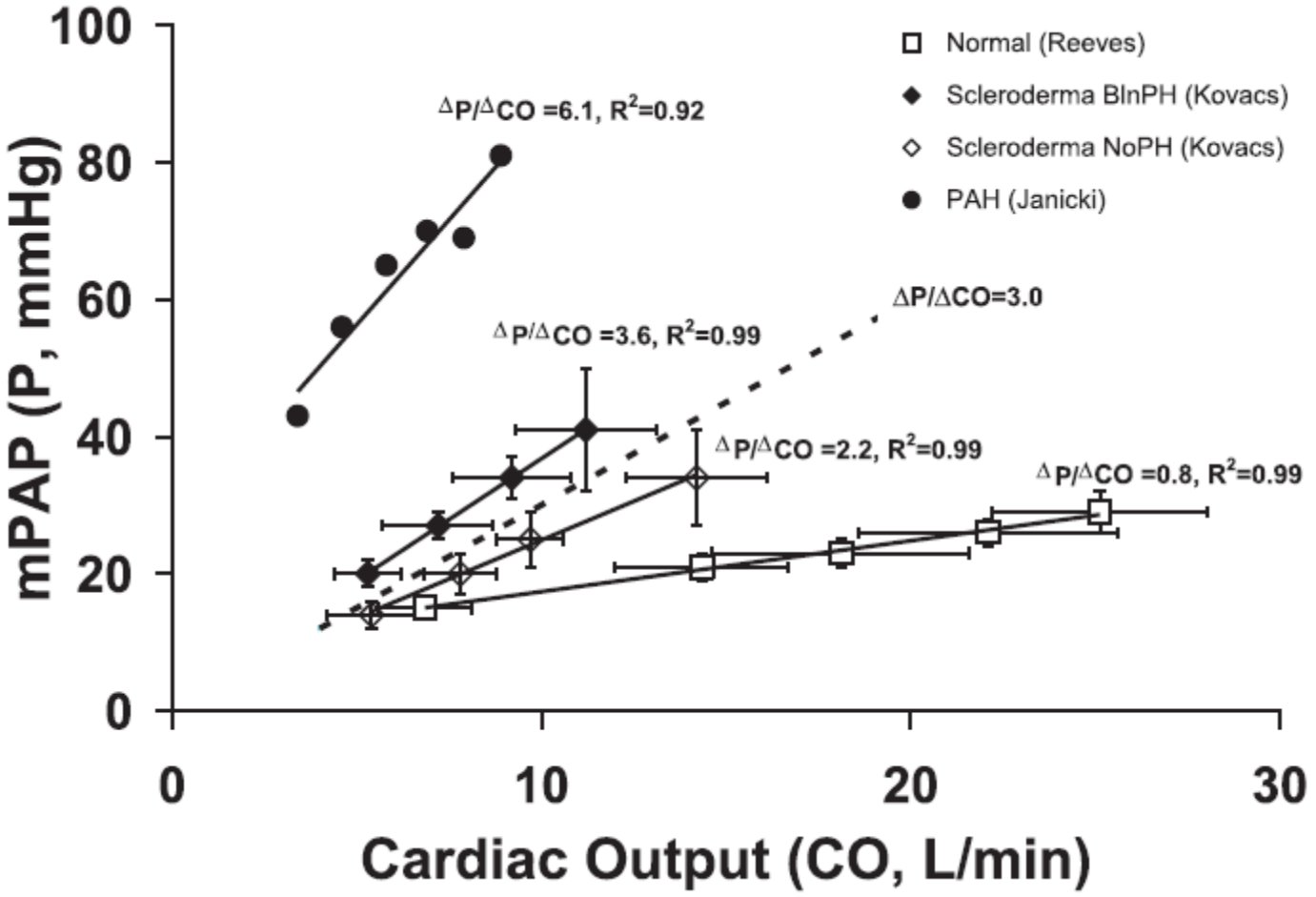
Tolle, Circulation 2008;118:2183

PA pressure normal response to exercise



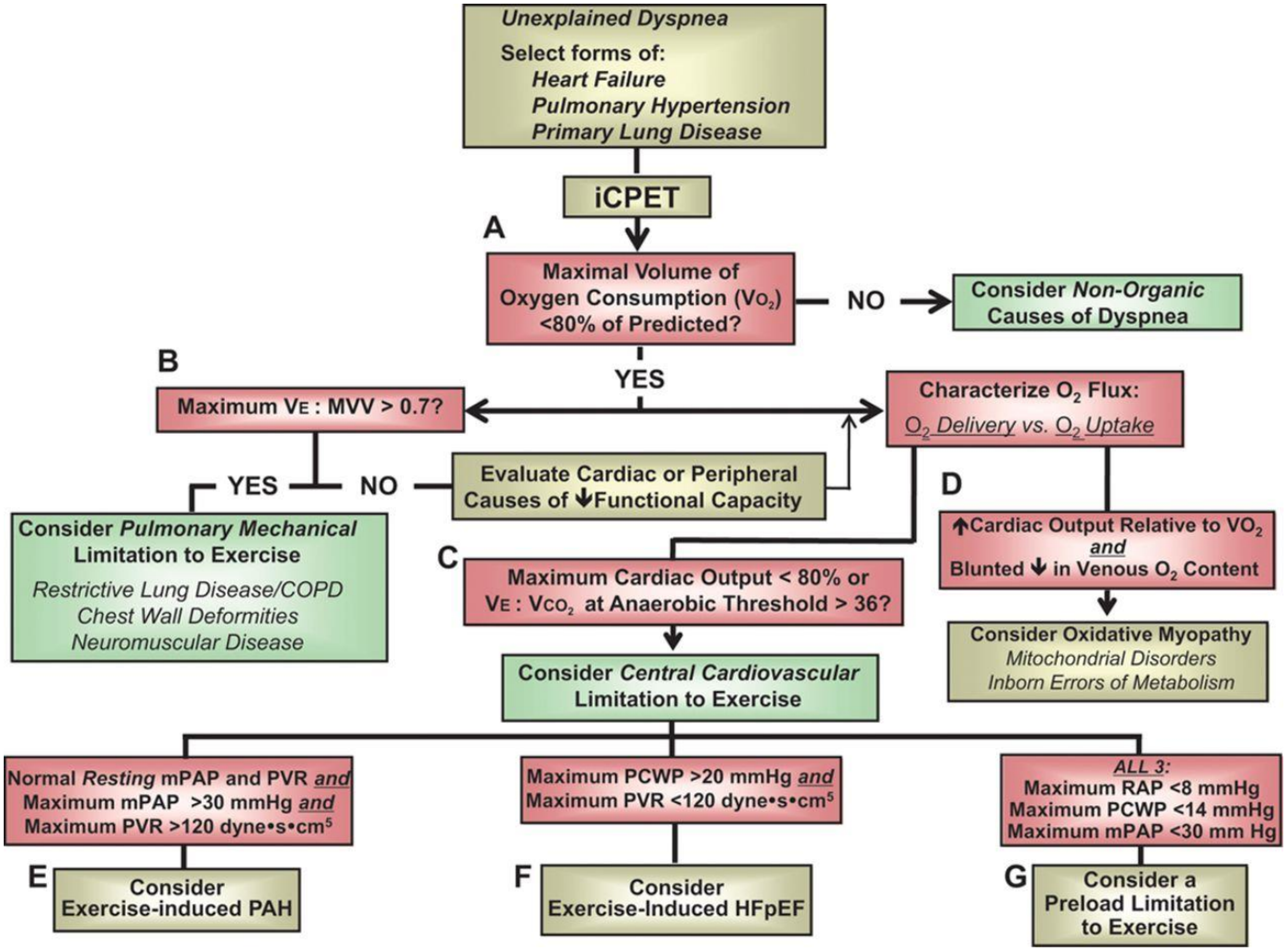
Lewis, Circ 2013:128;1470

Pulmonary Circulation Pressure-Volume Response to Exercise



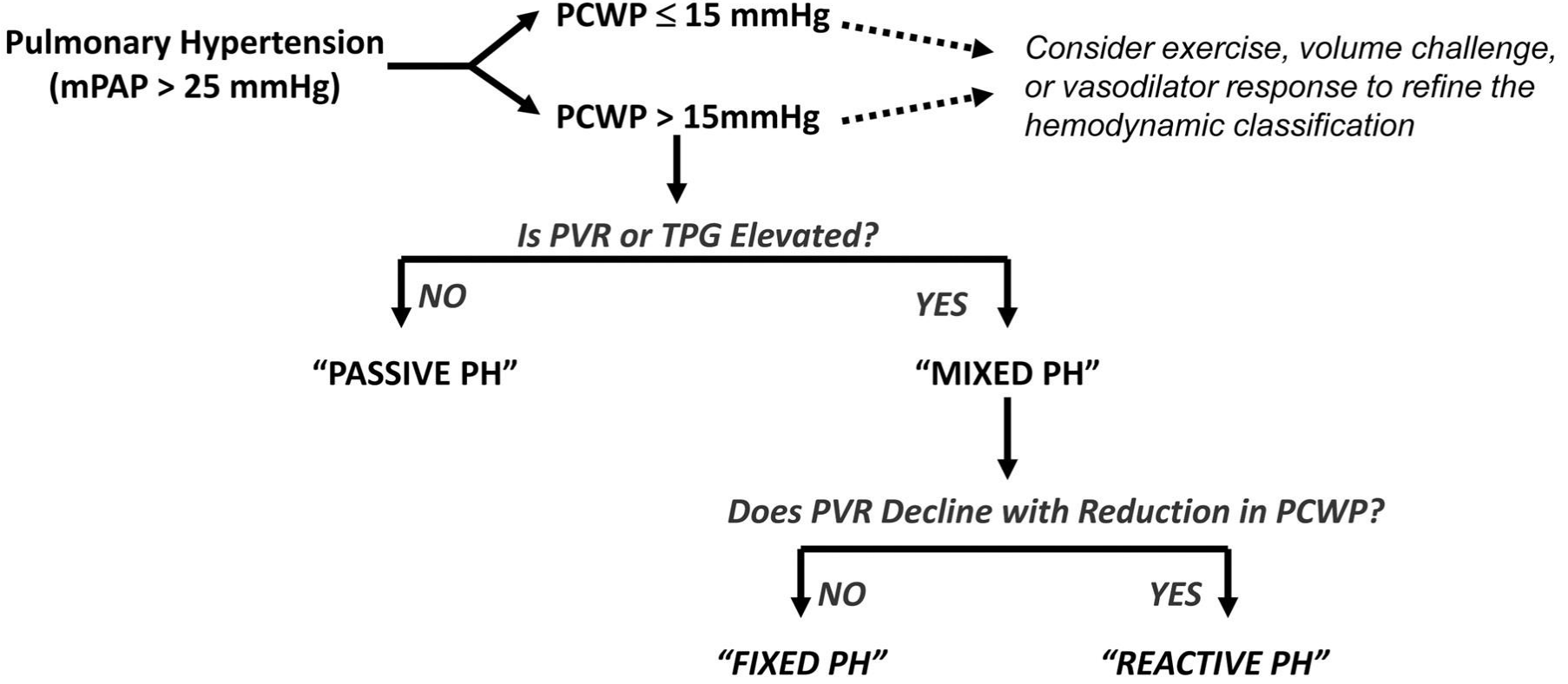
Lewis, Circ 2013:128;1470

A diagnostic algorithm for interpreting iCPET results.



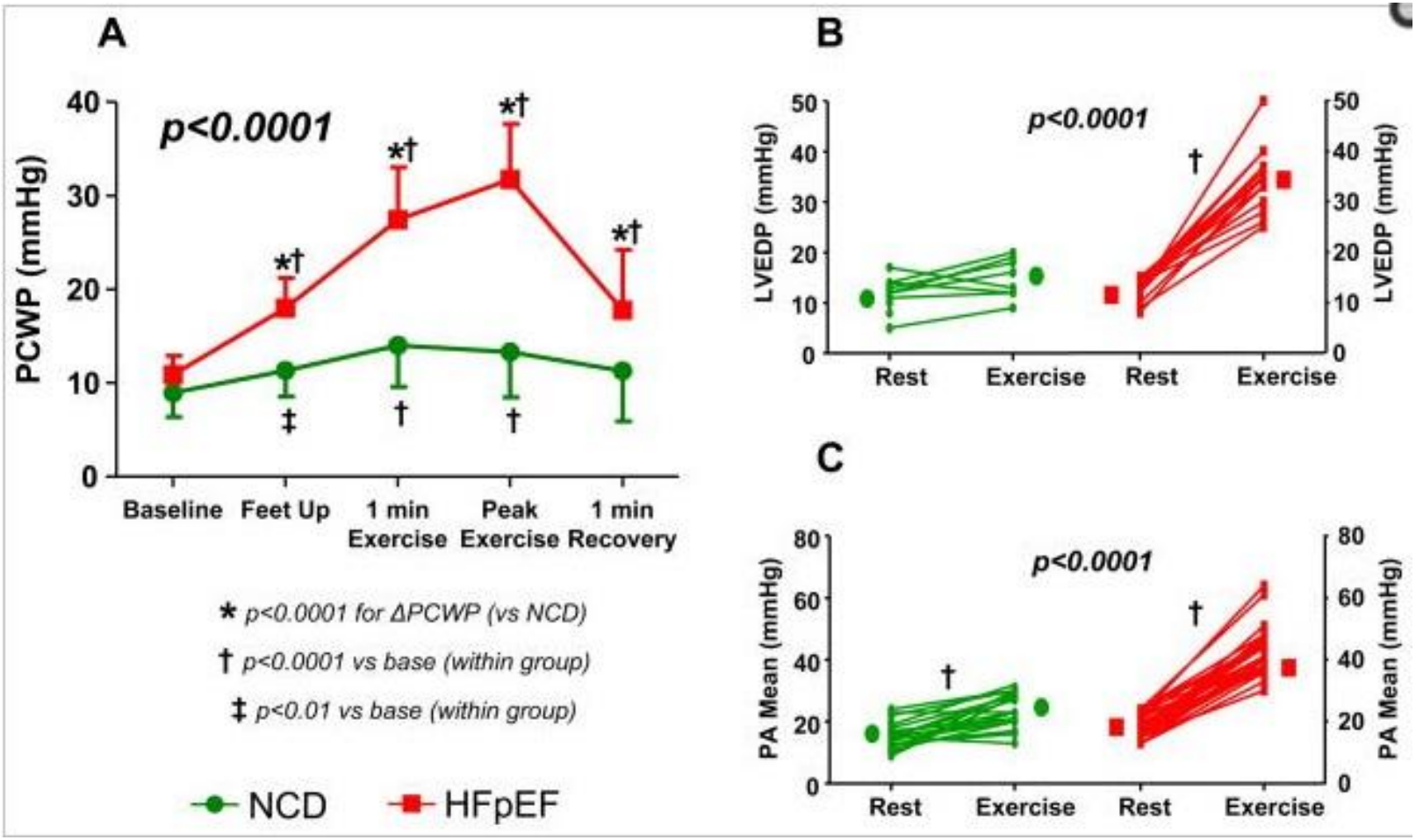
Maron B A et al. Circulation 2013;127:1157-1164

Diagnostic Framework for elevated PA pressure in Heart Failure



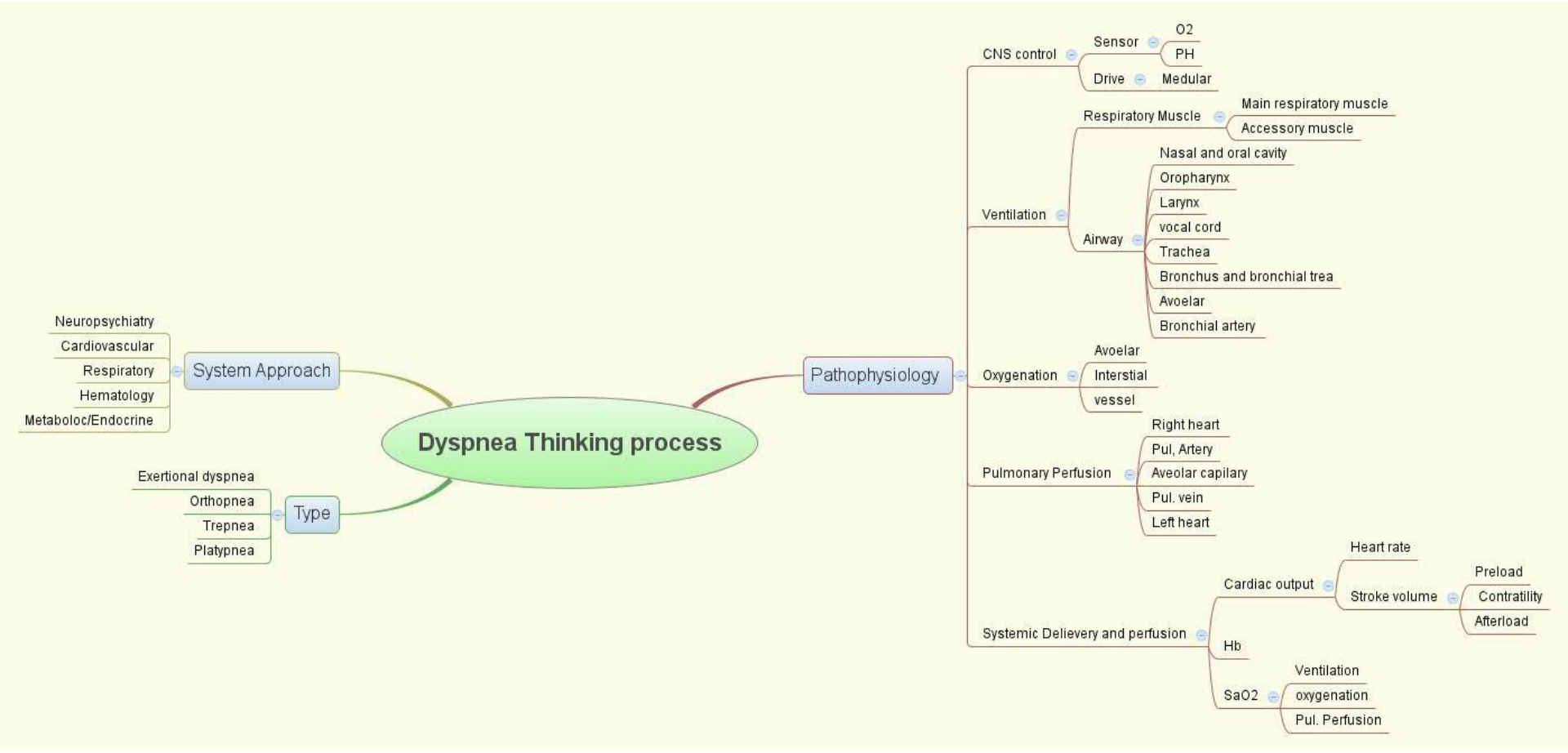
Lewis, Circ HF 2011:4;541

Exercise Hemodynamics of HFpEF



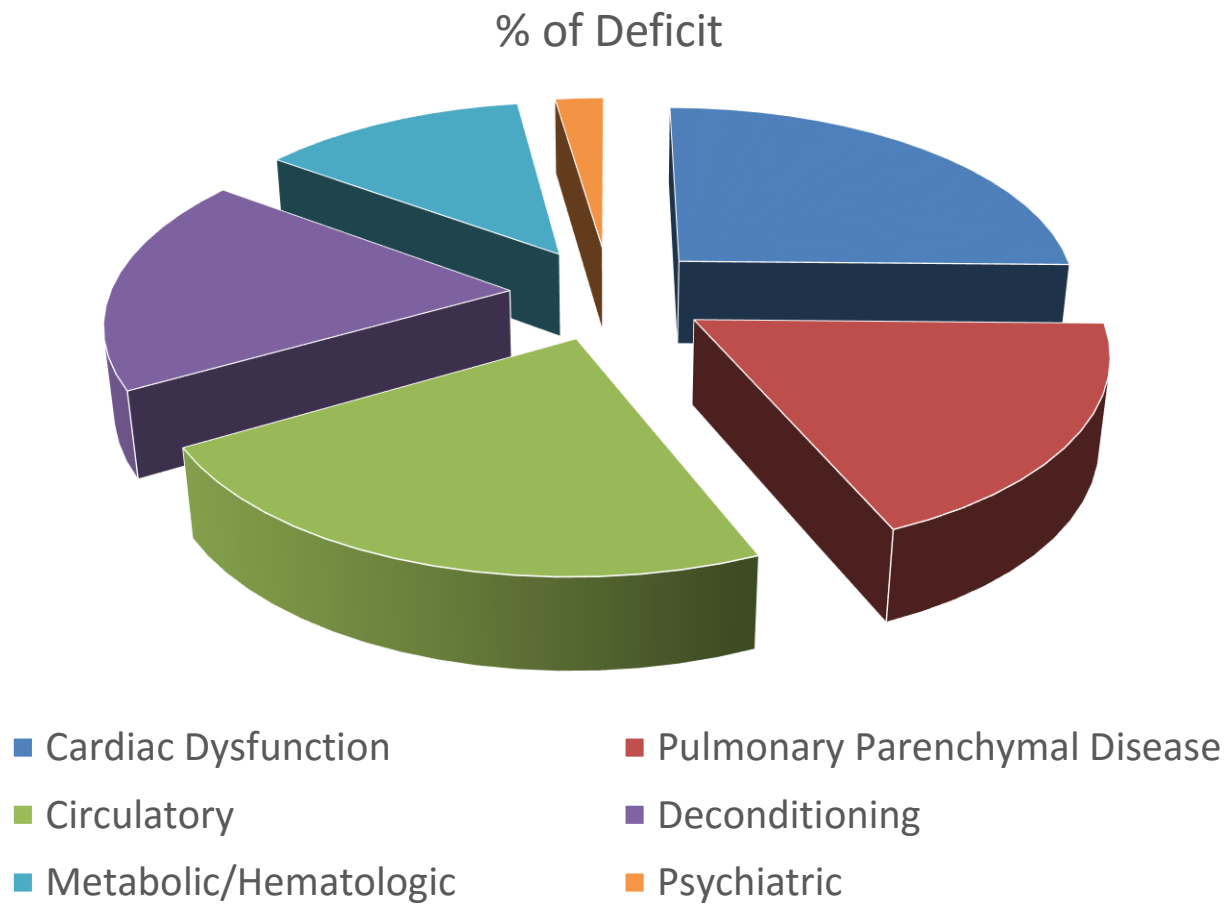
Borland, BA et al. Circ Heart Fail. 2010 Sep;3(5):588-95

UH Dyspnea Program, Summary and Conclusions



Pathophysiology for the Health Professions by Barbara E Gould

Alternate Approach to Cardiopulmonary Dysfunction



Causes of Dyspnea in UH Program

- Cardiac
  - Heart Failure (HFPEF)
  - Chronotropic incompetence
  - Undiagnosed critical coronary artery disease
  - Deconditioning
- Pulmonary and Airway
  - Asthma
  - IPF
  - Vocal Cord Dysfunction
- Others
  - Metabolic Acidemia
  - Probable mitochondrial abnormality
- Many Patients with multiple issues

Conclusions

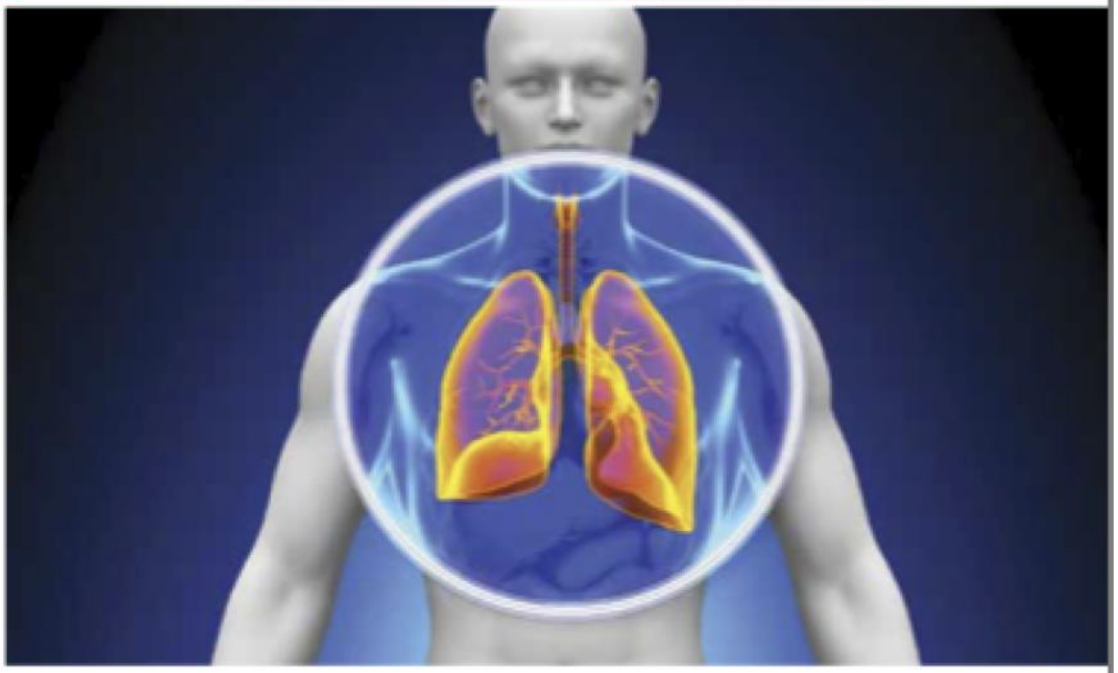
- Dyspnea is a symptom with multi-organ system origins
- A step-wise approach to the dyspneic patient improves diagnostic accuracy
- Exercise is the preferred stressor to differentiate cardiac and pulmonary causes.
- In patients with both heart and lung disease, invasive cardiopulmonary exercise allows for determining which is predominant.
- *Preliminary data suggests that exercise prescription based on testing and application of modern exercise training strategies may improve performance in the setting of difficult to manage cardiopulmonary disease.*

Mad magazine #60 in January 1961. Spy vs. Spy © 2001 E.C. Publications

University Hospitals
Harrington Heart & Vascular Institute

Cleveland | Ohio

Dyspnea Center



Referral Lines: 216-844-3800 or 216-844-2639