CPX 101: What heart failure nurses really need to know about cardiopulmonary testing

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Brief history

Joseph Priestly (1733-1804)

Discovers Oxygen
Nathan Zuntz (1847-1920)

Discovers method to collect air

Andre Cournande (1895–1988)
Dickson Richards (1895–1973)

• Nobel Prize winners in Medicine and Physiology
• Founders of modern cardiopulmonary medicine
• "the heart, lungs, and circulation really are a single functional unit; here are its normal values, this is how it works, and these are the manifestations of malfunction"

Cardiopulmonary Exercise Lab at UPENN

“Modern” air collection
CPX performed on cycle ergometer

Physiology

Basic gas exchange
Three phases of gas exchange

1. Breathing (ventilation)

2. Transport of O₂ and CO₂ in blood (circulation)

3. Exchange of gases within body cells (respiration)

Gas exchange expanded

Gas exchange with exercise

- Exercise requires the release of energy from the terminal phosphate bond of ATP for the muscles to contract.
- Aerobic oxidation of carbohydrates and fatty acids are the major source of ATP production, and
- Only source of ATP during sustained moderate exercise
- However this can only be sustained up to a point, then a second pathway is utilized
Gas exchange during exercise

- Glycolytic pathway uses glycogen to generate ATP
  - Produces ATP from glycogen – aerobic (does not need O2)
  - Very inefficient. Small amt energy for glycogen consumed
  - Consequence – lactate buildup

Oxygen Utilization (QO$_2$)

- Exercise results in ↑ oxygen utilization by muscles
  - ↑ oxygen extracted from blood
  - Dilatation of peripheral vascular beds
  - ↑ cardiac output
  - ↑ pulmonary blood flow
  - ↑ in ventilation

**In a perfect world: QO$_2$ = VO$_2$**

Oxygen Consumption VO$_2$

- The difference between the volume of gas inhaled and the volume of gas exhaled per unit of time.
- Determinants:
  - VO$_2$ interrelated to blood flow and O2 extraction
  - Fick equation
    - \( VO_2 = CO \times (CaO_2 - CvO_2) \)
    - CO = Cardiac Output
    - CaO$_2$ = arterial oxygen saturation
    - CvO$_2$ = venous oxygen saturation
VO2 Max
Maximum Oxygen Consumption

- Lungs: ventilation, gas exchange
- Heart: CO, SV, HR
- Circulation: pulmonary, peripheral, Hgb

VO2 Max
Maximum Oxygen Consumption

- VO2 increases linearly until SV, HR or tissue extraction approaches limitations – VO2 plateau
- VO2 Max is the point at which there is no further increase in VO2, despite further increases in workload.
- It is the best overall measure of CV fitness.
- Represents the upper limit of ATP production via aerobic metabolism

Anaerobic Threshold - AT

The VO2 at which anaerobic metabolism contributes significantly towards the production of ATP
Anaerobic Threshold - AT

- Non invasive estimate of cardiovascular function
- AT demarcates the upper limit of a range of exercise intensity that can be achieved aerobically
- Work rates below AT can be sustained indefinitely
- Work rates above AT is associated with progressive decrease in exercise tolerance

Interacting systems during exercise

Systemic impairments limiting exercise

- Obesity
- PAD
- Heart disease
  - CAD
  - CM
  - VHD
  - CHD
- Ventilatory disorders
  - Airflow obstruction
  - Restrictive lung dz
  - Chest wall defect
- Smoking

- Defect in Hg content and quality
- Metabolic acidosis
- Neuromuscular disease
- Glycolytic enzyme disorders
- Electron transport defects
- Anxiety
- Poor effort or manipulated performance


Cardiopulmonary Exercise Testing – CPX, aka CPET

Non invasive way to simultaneously test cardiovascular and ventilatory response to known exercise stress via measurement of gas exchange and utilization

Indication for CPX

• Evaluation of exertional dyspnea
• Development of an exercise prescription
• Direct measurement of functional capacity
• Risk stratification and prognosis in heart failure
• Optimization of rate-adaptive pacemaker
• Congenital heart disease: determination of need for surgical repair and response to treatment
• Disability determination: worksite readiness
• Assess functional significant or valvular heart disease


Contraindications for CPX

• Acute MI (3-5 days)
• Acute myocarditis
• Severe symptomatic aortic stenosis
• Decompensated heart failure
• Uncontrolled arrhythmia
• Dissecting aneurysm
• Resting SaO₂ <86%

Conducting the test

- Preparing the patient:
  - Education: many resources available, for example: Education website
  - History
  - Clinical exam
  - EKG
  - BP
  - O2 Sat
  - ABG
  - Preliminary PFT – spirometry
  - Treadmill vs bike

Parameters measured or derived from CPX

- Peak oxygen uptake (PkVO₂): Highest VO₂ achieved; generally occurring at peak exercise. (ml/kg/min)
- Maximal oxygen uptake (Max VO₂): Value achieved when VO₂ remains stable despite increase in exercise intensity (peak aerobic activity)
- Anaerobic threshold (AT): Exercise limit above which anaerobic energy production supplements aerobic metabolism.
- Breathing reserve (BR): Difference between maximum voluntary ventilation and the achieved maximum exercise minute ventilation
- Ventilation/carbon dioxide production ratio (VE/VCO₂): Also known as ventilatory equivalent to CO₂. Reflects chemoreceptor sensitivity, acid base balance and ventilatory efficiency.
- Respiratory exchange ratio (RER): Ratio of carbon dioxide output to oxygen uptake (VCO₂/VO₂)
- O2 pulse: Amount of oxygen consumed from the volume of blood delivered to tissue with each heartbeat.


Flow chart for the differential diagnosis of exertional dyspnea and fatigue.

[Flow chart image]

CPX in heart failure

- Essential component for evaluation for advanced therapies, LVAD, transplant
- VE/VCO2 slope may be valuable in determining prognosis
- CPX can be used to optimal interval timing in BiV non-responders
- Can be useful in assessing adequate physiologic response to medical therapy.

CPX TESTING IN HF

<table>
<thead>
<tr>
<th>Class</th>
<th>Severity</th>
<th>Max VO2 (ml/kg/min)</th>
<th>Max CO (L/min)</th>
<th>AT (ml/min/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>None to mild</td>
<td>&gt;20</td>
<td>&gt;8</td>
<td>&gt;14</td>
</tr>
<tr>
<td>B</td>
<td>Mild to moderate</td>
<td>16-20</td>
<td>6-8</td>
<td>11-14</td>
</tr>
<tr>
<td>C</td>
<td>Moderate to severe</td>
<td>10-15</td>
<td>4-6</td>
<td>8-11</td>
</tr>
<tr>
<td>D</td>
<td>Severe</td>
<td>6-9</td>
<td>2-4</td>
<td>&lt;10</td>
</tr>
</tbody>
</table>

Weber Classification for functional capacity

<table>
<thead>
<tr>
<th>CPET Variable</th>
<th>Description and Physiologic Relevance</th>
<th>Measurement Methodology</th>
<th>Required Exercise Duration</th>
<th>Threshold for Abnormal Prognostic Significance in Heart Failure</th>
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<tbody>
<tr>
<td>Peak VO2</td>
<td>aerobic capacity, gold standard indicator of maximum cardiorespiratory fitness. Highest VO2/average over 30s occurring in final minute of max exercise</td>
<td>Maximum VO2 achieved</td>
<td>90 sec</td>
<td>HR ≤ 80% predicted for mortality. 1 ml/kg/min decrease in VO2 peak leads to an 8% reduction in CV death &amp; HF hospitalization</td>
</tr>
<tr>
<td>VO2 uptake</td>
<td>phase I: initiation of exercise, Phase II: reflex peripheral muscle vasoconstriction, slow kinetics = higher VO2 debt</td>
<td>VO2 uptake (average over 30s) occurring in final minute of max exercise</td>
<td>90 sec</td>
<td>VO2 uptake ≤ 80% predicted for mortality. VO2 uptake &lt; 80% predicted leads to an 8% higher mortality</td>
</tr>
<tr>
<td>Anaerobic threshold</td>
<td>limit of aerobic metabolism during exercise, reflects metabolic switch to anaerobic metabolism</td>
<td>Maximum onset of expression of breath-by-breath VO2 production or VO2 consumption</td>
<td>90 sec</td>
<td>VO2 uptake ≤ 80% predicted for mortality. VO2 uptake &lt; 80% predicted leads to an 8% higher mortality</td>
</tr>
<tr>
<td>VO2 pulse</td>
<td>methods: premature latching or false brief pauses in response to exercise (e.g. cardiac rhythm, HR predominating)</td>
<td>VO2 pulse (per breath)</td>
<td>90 sec</td>
<td>VO2 pulse ≤ 80% predicted for mortality. VO2 pulse &lt; 80% predicted leads to an 8% higher mortality</td>
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Adapted from Malhotra, R. et al. J Am Coll Cardiol HF. 2016

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<td>Ventilatory efficiency</td>
<td>measure of ventilation required to exchange 1 L/min of CO2; reflects right ventricular-pulmonary vascular function and neural reflexes controlling ventilatory drive</td>
<td>Slope of least-squares regression of total minute ventilation (VE) against CO2 production</td>
<td>6 min</td>
<td>VE/VEE &gt; 34 leads to a 6-fold higher mortality at 18 months if &gt;34 in HF</td>
</tr>
<tr>
<td>Oscillatory ventilation</td>
<td>a distinct form of periodic breathing that reflects circulatory delay relative to metabolic needs during exercise.</td>
<td>3+ contiguous, regular oscillations in VE with amplitude ≥ 25% of VE, persisting for ≥ 60% of exercise</td>
<td>6 min</td>
<td>Oscillatory ventilation leads to a 3-fold higher mortality (&gt;20% 1-yr mortality)</td>
</tr>
<tr>
<td>OUES</td>
<td>slope (OUES)</td>
<td>VO2 uptake relative to ventilation (VE); a higher value reflects improved adaptation of the cardiopulmonary circuit to oxygenate and deliver blood for a given VE</td>
<td>6 min</td>
<td>OUES ≤ 1.47 leads to a 2-fold higher mortality</td>
</tr>
</tbody>
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**VE/VCO2 SLOPE**

Kaplan Meier analysis for 1-year cardiac-related mortality with VE/VCO2 slope threshold of 34. Log rank = 20.6, P < .0001.

Integrated Assessment of CPET Variables for Risk Stratification in HF


Risk Assessment – VE/VCO₂ & PetCO₂
Identify patients ‘at-risk’ for Readmission/Hospitalization

<table>
<thead>
<tr>
<th>Group</th>
<th>Characteristics</th>
<th>Subjects</th>
<th>Events</th>
<th>% Event Freq</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Resting PetCO₂ &gt;33 mmHg &amp; VE/VCO₂ slope &lt;34.4</td>
<td>48</td>
<td>4*</td>
<td>91.7%</td>
</tr>
<tr>
<td>B</td>
<td>Resting PetCO₂ =33 mmHg &amp; VE/VCO₂ slope ≥34.4</td>
<td>33</td>
<td>15**</td>
<td>54.5%</td>
</tr>
<tr>
<td>C</td>
<td>Resting PetCO₂ ≤33 mmHg &amp; VE/VCO₂ slope ≥34.4</td>
<td>40</td>
<td>31***</td>
<td>22.5%</td>
</tr>
</tbody>
</table>

*0 cardiac-related deaths, 4 hospitalizations; **2 cardiac-related deaths, 13 hospitalizations; ***7 cardiac-related deaths, 24 hospitalizations; ‡1 year


Mechanistic Basis for Ventilatory Instability/Inefficiency in Heart Failure

Exercise Risk Score

Cumulative survival by Kaplan-Meier analysis for composite risk scores. P < .001 by log-rank test.

Cumulative cardiovascular event-free survival Kaplan-Meier analysis for composite risk scores. Cardiovascular events were death, transplantation, LVAD implantation, and CHF hospitalization. P < .001 by log-rank test.