Triennial Pulmonary Workshop 2015

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**Terminology**

**PFTs:** Pulmonary Function Tests

**FVC** = Forced Vital Capacity (total volume of air exhaled in a forced exhalation from total inspiration to total exhalation -- ideally with the best of three efforts recorded)

**FEV1** = Forced Expiratory Volume in 1 second (total volume of air exhaled in the first second of a FVC maneuver -- ideally should be 6 seconds or more of exhalation effort with the best of three efforts recorded)

**FEF25-75** = Forced Expiratory Flow in the 25th to 75th portion of flow-volume curve (also sometimes listed as MMEF 25-75: Maximal Mid-expiratory Flow 25th to 75th portion of the flow volume curve)

**EF** = Ejection Fraction (of the Left Ventricle)

**TLC** = Total Lung Capacity

**FRC** = Functional Residual Capacity (amount of air in the lung at end-of-normal tidal volume exhalation)

**DLCO** = Diffusion of Lung to Carbon Monoxide
### SPIROMETRY

#### FEV1/FVC

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#### FEF25-75%

Volume change per second = Flow

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Flow-Volume Loops

Flow

Volume

Flow-Volume Loops

Flow

Volume

Airway Obstruction
Flow-Volume Loops

As obstruction worsens, the expiratory limb "caves in" more and more.

Flow-Volume Loops

Restriction – a "miniaturization" of a normal flow-volume loop.
Flow-Volume Loops

Extra-thoracic Airway Obstruction (laryngeal, upper tracheal)

Plateauing of inspiratory loop

Flow-Volume Loops

Fixed airway obstruction (tracheal, carinal obstruction)
Case 1: Obstructive Lung Diseases

45 year old male

- Undergoes routine medical testing for Life insurance application
- Discloses childhood asthma
- Medications: None
- Never smoked
- Physical exam: Appears well, not in any obvious distress, BP 110/80, pulse 80, respiration 14
- Lung exam clear
- CXR normal
- Spirometry: FVC 98 % predicted, FEV1 74 % predicted, FEV1/FVC 65 %, and FEF 25-75 42 % predicted. Volume expired (Y axis) vs. Time (X axis) shows exhalation for 4 seconds
- Current EKG and Stress Test – Normal resting EKG, Stress test – Bruce Protocol, exercise time 8:30 min, achieved 96% MPHR, peak HR 169, peak BP 135/60, test stopped due to target HR achieved, negative for ischemia

Questions:
1) Describe your initial thoughts on the client’s medical history and test results

Clinically, the client’s self-reported history of asthma seems to be asymptomatic. He does not use inhalers regularly, his lung exam is clear, his CXR does not show hyperinflation, his exercise capacity is reasonable (8:30 min Bruce Protocol), and exercise is not limited by shortness of breath.

2) What does the spirometry show? How does the duration of exhalation time affect the results?

Spirometry gives the FEV1, FVC, and FEF 25-75 values.
The client’s spirometry shows mild obstruction, but no post-bronchodilator FEV1 was reported, so reversibility was not assessed. If, in this case, the FEV1 increased to 85% predicted following bronchodilator treatment, then that would indicate essentially complete reversibility consistent with asthma.

In general, exhalation time of at least 6 seconds is optimal, but this client exhaled for 4 seconds, which may underestimate the FVC (see answer to question #4 below).

3) Does this client have asthma? Cite evidence to support your view. Does the CXR or Stress test help you?

Presuming post-bronchodilator FEV1 increased to 85% predicted, he has mild reversible obstruction on spirometry consistent with asthma, but he is clinically asymptomatic.

The clear lung exam, normal CXR, and good exercise capacity imply that his asthma is asymptomatic.

4) What if this client were a current smoker, ½ pack per day x 20 years? How does that affect your interpretation of the spirometry and medical history?

One would want to know the FEV1 post-bronchodilator treatment to determine the degree of reversibility. Irreversible obstruction or incomplete reversibility would indicate COPD. If FEV1 post-bronchodilator were 75% predicted in this case, then it would indicate irreversible obstruction and suspicion of mild COPD.

Factors to consider: Was the spirometry done when he was symptomatic or was it done when he was at her baseline (“at his very best”)? Was it done in a pulmonologist’s office or in a hospital PFT lab? Did the spirometry meet ATS criteria for a valid study?

From ATS/ERS Task Force: Standardization of Lung Function Testing. Eur Respir J 2005; 26: 319-228. Defines "good start" as extrapolated volume of < 5% of FVC or 150 cc, whichever is greater. For manual systems, the back extrapolation method traces back from the steepest slope on the volume-time curve. For computerized systems, the back extrapolation slope comes from the largest slope averaged over an 80 ms period. Satisfactory finish includes effort duration > 6 sec adults (> 3 sec children) and with computerized systems the system should indicate to tester when the volume-time curve shows no change in volume (<25 cc) for > 1 second. There should be a minimum of 3 efforts, with two of the efforts showing less than 150 cc difference in both the FVC and FEV1 efforts. If this criteria is not met, then additional efforts are needed until two of the efforts show < 150 cc variation in FVC and FEV1.

All of these factors can contribute to either misleading or unreliable spirometry results.

5) What are the differences between Asthma and COPD?
Asthma demonstrates complete reversibility of obstruction on PFTs, whereas COPD demonstrates incomplete reversibility, if any at all.

6) What would full PFTs generally be expected to show in Asthma and COPD?

For Asthma: Hyperinflated lungs with normal diffusing capacity, such as:
- TLC = 103% predicted
- FRC = 153% predicted
- DLCO = 98% predicted

For COPD: Hyperinflated lungs, diffusing capacity may be normal in early COPD, and low in later stages of emphysema, such as:
- TLC = 103% predicted
- FRC = 153% predicted
- DLCO = 58% predicted

Of note: In some cases of asthma, irreversible obstruction may occur after many years, as a result of remodeling of the airways over time.

7) What changes may be seen on CXR in acute asthma exacerbation, and what changes on CXR typically occur in COPD?

In asthma, the CXR may show hyperinflation.

In later stages of COPD, the CXR may show barrel-shaped chest, hyperinflated lungs, and flattening of the diaphragms. CXR may also show bullous changes of the lung.

8) Describe the underwriting approach for assessing the mortality risk of obstructive lung disease, in the first non-smoker client and the second smoker client? How does the mortality risk of each client compare to a standard insured population?

In the first case, the client appears to have mild asthma which seems to be clinically asymptomatic. His mortality risk would be similar to a standard insured population.

In the second case, the client has mild COPD and continues to smoke. He is relatively young, but already has early COPD. However, his exercise capacity is reasonable and his CXR is normal. His mortality risk would be mildly substandard compared to a standard insured population.
Case 2: Central Sleep Apnea (CSA) and Obstructive Sleep Apnea (OSA)

75 year old obese male (BMI 35 kg/m²)
- Symptoms: SOB / DOE, fatigue, daytime sleepiness
- PMH: Hypertension, MI, s/p 3 v. CABG, Type 2 DM
- Non-smoker
- Medications: Lisinopril, Spironolactone, Carvedilol, Furosemide, Insulin,
- Physical Exam: Appears somewhat sleepy, but answers questions appropriately
- Resting O₂ saturation on room air (RA) = 93%
- Physical Exam: Retrognathic chin, long soft palate, prominent tonsils and long uvula, deviated nasal septum
- Lung exam bibasilar rales
- Heart Regular rate and rhythm, S₁, S₂, faint systolic murmur
- Extremities 2+ pitting lower extremity edema.

Overnight Polysomnography (Sleep Study):
Total Sleep Time = 300 minutes (5 hours)
Sleep Latency = 5 minutes
REM Latency = 125 minutes
Total REM Sleep = 30 minutes
% REM Sleep = 10 %
Total Obstructive Apneas = 5
Total Obstructive Hypopneas = 5
Total Central Apneas = 15
Total Central Hypopneas = 10
Baseline O₂ sat RA = 93%, Lowest O₂ sat = 70%
30 % of sleep occurred with O₂ sat < 89%
Heart Rate Lowest 30 bpm, occasional PACs and PVCs,
Apnea Hypopnea Index = 7 events / hour
Also noted: Episodes of Cheyne-Stokes breathing
Titration with CPAP was initiated, and pressure was increased, but resulted in increasing number and length of central events. Titration with BiPAP was then undertaken with a default respiratory rate setting of 14, and optimal titration was achieved with I/E PAP of 20/8 cm H₂O
**CXR:** prominent heart shadow, increased interstitial markings

**Client’s PFTs:**
FEV1 = 73% predicted  
FVC = 74% predicted  
FEV1/FVC = 99%  
TLC = 76% predicted  
FRC = 62% predicted  
DLCO = 57% predicted

**Echocardiogram:** mild LVH, biventricular enlargement, global hypokinesis, LVEF 35 %, right ventricular systolic pressure (RVSP) = 50 mm Hg, moderate TR and mild MR

**Questions:**
1) What are the significant findings on the sleep study? Comment on the O2 desaturation seen on the sleep study. What might you see on an arterial blood gas (ABG)?

The significant findings are the presence of mainly central apneas and hypopneas, with a smaller amount of obstructive events occurring throughout sleep, associated with oxygen desaturation. Also noted is the presence of Cheyne–Stokes respiration (central apneas that occur during the decrescendo part of the cyclic crescendo-decrencendo respiratory pattern), which is associated with congestive heart failure (CHF). Since the events are mainly central, non-invasive ventilation with a backup respiratory rate setting was used for treatment.

The baseline O2 saturation is at the low end of normal, and the O2 desaturations into the 70s % are lower than usual. This implies underlying hypoxemia at baseline, presumably related to CHF and pulmonary hypertension.

An ABG may show low pO2, elevated pCO2, and low end of normal range O2 % saturation.

2) What do his PFTs show? What does the CXR suggest?

PFTs show mild restriction with low diffusing capacity.

The CXR suggests CHF.

3) What does the echocardiogram show?
The echocardiogram shows left and right heart disease. The left heart disease is dilated LV, global hypokinesis, and low LVEF with CHF, presumably secondary to CAD / MI. The right heart disease is pulmonary hypertension and dilated RV, which may be due to left heart disease.

Of note: In cases of severe OSA without underlying left heart disease, right heart disease may develop secondary to untreated severe OSA, which causes persistent hypoxemia, leading to pulmonary hypertension and right heart failure.

4) What is this client’s primary problem?

This client’s main medical problem is ischemic cardiomyopathy with CHF -- Left heart disease, CAD / MI, with CHF, resulting in mainly central sleep apnea. He has a minor component of obstructive respiratory events during sleep.

5) Comment on the treatment of his sleep disordered breathing. Why is there a default respiratory rate setting? What other options are available for treatment?

The treatment for this client would focus on the presence of central apneas due to underlying CHF. The treatment would be non-invasive ventilation, with an inspiratory and expiratory pressure setting and a back-up respiratory rate setting, to initiate breaths if he does not on his own. In this case, treatment would also be aimed at improving his cardiac status (i.e. treating LV dysfunction and CHF).

In general, treatment for CSA includes CPAP, supplemental O2, Adaptive servo-ventilation (ASV), and BiPAP with backup respiratory rate. In more severe cases, other types of ventilator support may be considered. Pharmacologic therapy, if indicated, includes respiratory stimulants such as acetazolamide or theophylline.

6) Describe various causes of central apnea, prognosis, and mortality risk

CSA may be primary (idiopathic CSA) or secondary to an underlying medical condition, such as a history of CHF or cerebrovascular accident (CVA). Central respiratory events may also be seen in high altitude periodic breathing, or may be secondary to medications or substances which depress respiration, such as opioid medications.

The prognosis and mortality risks of each cause are determined by the severity (and potential reversibility) of the underlying medical conditions.

7) Define Apnea, Hypopnea, and Respiratory Effort Related Arousal (RERA).

An “Apnea is defined as the complete cessation of airflow for a minimum of 10 seconds regardless of whether or not there is associated oxygen desaturation or sleep fragmentation (electroencephalographically defined arousal), although they are usually present,”* and a “Hypopnea has not been universally accepted, but it is
common to use a 30% or greater reduction in airflow associated with at least a 3% to 4% drop in oxygen saturation or an EEG alpha wave arousal.”


Respiratory Effort Related Arousal (RERA) – Disordered breathing event associated with arousal, but not meeting criteria for apnea or hypopnea.

8) Define obstructive and central events

An obstructive event is one in which there is an attempt made to breathe, but airflow is unsuccessful because of obstruction in the upper airway.

A central event is one in which there is no attempt made to breathe.

9) Describe the calculation of AHI and RDI

AHI: Calculation of number of apneas and hypopneas divided by total sleep time in hours

RDI: Calculation of number of apneas, hypopneas and RERAs divided by total sleep time in hours

In this case, the AHI = 5 OA + 5 OH + 15 CA + 10 CH / 5 hours = 35 / 5 = 7

Since there are no RERAs, the AHI = RDI in this case

10) Describe the features of OSA, including clinical symptoms, physical findings, and expected results on a sleep study

OSA: Characterized by periodic pauses in breathing during sleep, in which there is respiratory effort, but no airflow. Common signs and symptoms include snoring, witnessed apneas, and excessive daytime sleepiness. It is often associated with obesity (80%), narrowed airway, and retrognathic chin. In addition, CO2 retention and hypoxemia during wakefulness, pulmonary hypertension with right heart failure may be seen in more severe cases.

Overnight sleep study would show the presence of > 5 obstructive respiratory events / hour of sleep (see answers to questions above for definitions).

11) Explain what an Epworth Sleepiness Scale Score (ESS) is

The ESS is a measure of sleepiness in everyday life situations, which can be used as a screening test for excessive daytime sleepiness. It is scored from 0 to 24, and a score greater than 10 is consistent with excessive sleepiness.

12) In cases of OSA, how would you assess compliance with CPAP treatment?
Often one can download data from the CPAP machine which gives the number of hours of usage and other historical information. Guidelines used for compliance generally require a minimum of 4.5 hours of usage per night.

13) What are the appropriate treatments for OSA?

Weight loss for overweight individuals with OSA should be recommended. In this case, treatment with continuous positive airway pressure (CPAP) or bi-level positive airway pressure (BiPAP) should also be considered. Surgical intervention includes uvulopalatopharyngoplasty (UPPP) and jaw advancement surgery, which have had limited success. Dental appliances are sometimes used to reposition the jaw, but this treatment also has had limited success. A newer treatment being tested is hypoglossal nerve stimulation via an implantable device.

14) What are the expected outcomes for OSA treated with CPAP and for OSA not treated with CPAP?

CPAP is expected to improve the client’s symptoms of daytime sleepiness, improve the right heart disease, and protect against further adverse cardiovascular consequences of OSA.

If untreated, OSA has been associated with the development of cardiovascular impairments, such as hypertension, cardiac arrhythmias, and possibly cerebrovascular events. Also, there is a higher risk of injury related to accidents because of excessive daytime sleepiness.

15) Define the mortality risks associated in general with OSA and CSA compared to a standard insured population.

For OSA: Treated OSA would be associated with very close to standard to mildly substandard risk at most. Untreated OSA would be associated with high mortality risk in comparison to a standard insured population.

For CSA: If due to cardiac disease / CHF, the mortality risk would be related to the degree of underlying heart disease with generally high mortality risk in comparison to a standard insured population. In general, the mortality risks are determined by the cause.
Case #3: Interstitial Lung Disease

A 56 year-old male applicant for life insurance

- Listed on his application that he had seen his primary care physician within the previous 6 months
- An APS was requested and revealed that the applicant had been seen for a dry, non-productive cough and worsening shortness-of-breath especially with exertion
- Spirometry had been done in the office and revealed:

FVC 68% predicted
FEV1 71% predicted
FEV1/FVC 99%
FEF25-75 126% predicted

- What is the spirometric diagnosis?
  1. RESTRICTION (or restrictive defect) with the supra-normal FEF25-75% suggesting good patient effort (and no airway obstruction).
  2. Complete Pulmonary Function testing is always required to validate “Restriction” on spirometry
- Would that diagnosis change if the FEF25-75 were 52% predicted instead?
  1. Still RESTRICTION but the likelihood of poor patient effort vs. concomitant minimal-to-mild airway obstruction is raised

Review of the PCP’s APS revealed that the applicant had been referred to a cardiologist when physical examination revealed bibasilar crackles on auscultation. The cardiac evaluation confirmed the physical findings and revealed a CXR read by the radiologist as “Congestive Heart Failure”. Echocardiogram revealed an estimated EF of 55% with Grade 1 diastolic dysfunction and was otherwise normal. The patient underwent Left Heart Catheterization with coronary angiography found to have minimal obstructive lesions and LVEDP of 12.

The cardiologist referred the applicant to a tertiary medical center hospital’s Pulmonary Function Laboratory where complete PFTs revealed similar spirometry but also:

TLC 76% predicted
FRC by plethysmography 81% predicted
DLCO 42% predicted

- What diagnosis would these findings suggest?
- RESTRICTION with decreased lung diffusion (DLCO) – confirmed restriction with reduced lung volumes and reduced lung diffusion is consistent with interstitial lung disease

- What further studies would be sought in the medical record (or required before further underwriting could be done?)
  - Chest radiograph, CT imaging (preferably HRCT imaging), possibly a VATS lung biopsy (or at least fiberoptic bronchoscopy with transbronchial lung biopsy)

- Assume complete PFTs are available for review. Would your diagnosis change if the FEF25-75 were instead 85% predicted and the TLC remained 76% predicted but the FRC was normal (98% predicted) and DLCO 42% predicted?
  - This would suggest normal lung function, with the TLC below normal simply because of inadequate effort on the IC (Inspiratory Capacity) maneuver. Remember that TLC is FRC (actually measured w/o effort concerns) + IC (inspiratory capacity, requiring considerable effort)
  - Much more importantly however is the fact that the DLCO is 42% of predicted in the setting of normal or near-normal spirometry and measured lung volumes. This strongly correlates with pulmonary vascular disease – occult pulmonary thromboemboli (or other pulmonary embolic events) and/or pulmonary hypertension. V/Q scan, CT angiogram, and/or echocardiogram would be needed for further inquiry.

- Would your diagnosis change if the Spirometry was 70% of normal and the TLC and FRC were correspondingly reduced but the DLCO was normal?
  - This would suggest RESTRICTION on PFT due to non-lung causes – ie, kyphosis or scoliosis, neuromuscular diseases, pleural effusion, prior resection of lung, etc

- Discuss the different types of restrictive lung disease in terms of the clinical presentation, laboratory and radiographic findings, clinical course and prognosis, underwriting approach, and mortality risk compared to a standard insured population.
Case #4: The solitary pulmonary nodule

A 56 year-old male applicant for life insurance

• Revealed on his application that he had a 30 pack year history of smoking but had quit smoking 5 years prior to application.
• He disclosed that he had just recently undergone low-dose CT Lung screening and had been found to have a 9 mm nodule in his left upper lung.
• He explained on the comments section of the application that his physician had explained that the nodule was “almost certainly benign” but that his physician was planning to repeat the CT lung in one year “just to be sure”.

Assuming that the radiology report of the CT scan (and/or a copy of the CT lung on CD) was available, what findings might allow underwriting to proceed with a possible favorable underwriting decision?

• The pulmonologist’s gospel is always always look and see if any old CXRs can be found. If the nodule is seen and is same-size on a film > 2 years old, then the nodule may be assumed to be benign and requires no debits or further follow-up
• Assuming that the case is postponed (for lack of favorable characteristics of the nodule), when might a decision be made assuming correct surveillance of the nodule is done? What constitutes an appropriate surveillance of such nodules?
  o Again, 2+ years of stability (size and appearance) defines the nodule as benign.

Additional considerations:

• Would your opinion change if the nodule were 3.5 cm instead?
  o Absolutely. Any lung density 3+ cm is correctly named “mass” instead of nodule, and should be considered malignant until proven otherwise
• What if the nodule had been evaluated with PET/CT imaging and found to have an SUV of 1.0 (ie, the nodule was FDG non-avid)?
  o First consideration if that PET/CT imaging falls in sensitivity for uptake below 1 cm, so imaging nodules < 1 cm is not as helpful in either ruling in or ruling out a malignant diagnosis
  o Remember also that serum glucose must absolutely be measured before this test is done, especially in diabetics. High levels of glucose (> 200 mg/dL) invalidate the test because of competitive binding of the FDG molecule’s ability to bind in setting of hyperglycemia
  o All that being said, a nodule with low SUV is seen usually with a benign lesion and if malignant, the lesion is very slow-growing.
• What if fiberoptic bronchoscopy had been done with negative results, and the applicant had then undergone VATs open lung segmental resection with pathology findings negative for any diagnosis other than “normal lung”?
Unfortunately neither the applicant nor the medical underwriter are helped with this result. The nodule would be expected to have some “nodule” pathology, either benign or malignant. “Normal lung” would suggest that the nodule was not in fact removed in the lung resected. It happens often enough that invasive pulmonologists doing navigation bronchoscopy place fiducial markers as near to the lesion as possible, both to help the surgeon find the lesion or to serve as a target for Cyberknife or other radiology.

- **Other comments about solitary pulmonary nodules**
  - Technically, an SPN is a lung lesion that is completely surrounded by lung and pleural-based nodules are not technically SPN’s (and generally carry a less-significant prognosis)
  - CT imaging of the lung and abdomen is now done so frequently and with ever more sensitive machines that the likelihood of finding some incidentaloma may be as high as 40%
  - Many of these nodules will be 3 mm or less and current Fleischner Guidelines (Radiology) does not mandate following these with further CT imaging in low-risk persons (younger age, non-smokers, no history of workplace exposure to potential carcinogens, no familial history of malignancies, etc)
  - Nodules with very smooth and well-defined margins are much less likely to be malignant, as opposed to nodules that are “speculated” or associated with GGO (ground-glass opacification)
  - As a general rule, upper lobe nodules are more worrisome for malignancy than lower lobe nodules
  - There are certain characteristics of nodules that would allow immediate (and favorable) consideration by underwriters without follow-up or further concern. These include:
    - Diffusely or heavily calcifies nodules (these will be read out by radiologist as “calcified granulomas”) → these are totally benign
    - Nodules with central calcification (“bulls-eye” nodules)
    - Nodules with laminated calcification rings
    - “Popcorn” calcification within the nodule (but note that nodules with eccentric calcification are considered high-risk for malignancy
  - **SPN calculators are readily available**
    - Just Google “SPN Calculator” and there will be found a number of calculators of risk of malignancy based on age, smoking history, concomitant emphysema, etc.
References:

See references previously listed in other handouts

uptodate.com

emedicine.medscape.com

Textbook of Pulmonary Medicine:


Textbook of Sleep Medicine:


Textbook of Insurance Medicine: