Integration of Clinical Findings and Physiology in Respiratory Disease

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Respiratory diseases have broad category from allergic disease to diffuse lung diseases. In approach for these diseases, we should collect many useful clinical information with physiological, imaging, and pathological point of view. Using focused clinical approach and physiological thinking will contribute to arrive adequate diagnosis with imaging and pathology. I show integrated approach of clinical findings and physiology for representative respiratory diseases such as community acquired pneumonia, chronic obstructive lung disease, bronchial asthma and interstitial lung disease.

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Abbreviation
FVC: forced vital capacity; DLco: Diffusing capacity of the lung for carbon monoxide; 6MWTD: 6 minute walking test distance; 6MWTD; mMRC: modified Medical Research Council.

Diagnosis and management of respiratory disease is based on detailed history, physical examination and physiology. However, there are scarce reports about integration of clinical information and physiological findings.

I describe practical approach for common respiratory diseases using clinical findings and physiological data.

First, I show approach for community acquired pneumonia. In history taking, clinical course is most crucial. I divide into three courses such as acute, subacute and chronic. These clinical scenario is associated with likely infection. For example, representative acute pneumonia are pneumococcus, Klebsiella, Legionella, influenza virus and aspiration pneumonia. Subacute community acquired pneumonia are Hemophilus influenzae, Moraxella catarrhalis and mycoplasma pneumonia (Table 1).

If we see chronic pneumonia, important differential diagnosis are tuberculosis, lung abscess and actinomycosis.

In terms of physical examination, oral hygiene contribute to respiratory infection especially anaerobic infection such as aspiration pneumonia, lung abscess and empyema. Lung auscultation provide useful information for physician. When we hear pan-inspiratory crackles, our priority diagnosis is typical pneumonia with non-segmental distribution such as pneumococcal pneumonia and Klebsiella pneumonia. On the other hand, if we hear late inspiratory crackles, we usually consider atypical agent such as mycoplasma, legionella or viral pneumonia. Extra-pulmonary symptoms such as joint pain, muscle ache and rash reminds us about mycoplasma and viral infection.

Regarding physiology of respiratory infection, chest echo is recent useful tool. It clarifies definite pleural effusion with internal structure. When we see patients who has persistent fever with adequate antibiotics, one of the differential diagnosis is para-pneumonic effusion. With echo, I recommend thoracocentesis if free fluid is over 2 cm and fibrin like material within fluid suggest...
In terms of physical examination, orthopnea is significant in asthma. Obesity and chronic sinusitis contribute (Table 3). Environmental factors. After 12, adult onset asthma is possible, childhood asthma is likely and usually associated with atopy and accompanied with bicarbonate from proximal renal tubule. Facial and leg edema is associated with cor pulmonale or chronic sign and this means chronic lean forward posture of patients. Chronic inflammation of more central airways. In peripheral muscle, these sounds correspond to hyperinflation, severe air-trapping and distant or early crackles, and early-to-mid inspiratory crackles. Impairment of inspiratory muscle activity. Percussion of lung reveal of sterno-cleido muscles because of dysfunction of diaphragm and of chronic respiratory diseases. COPD patients show hypertrophy of polycythemia due to chronic hypoxemia. Neck has much information.

In terms of physical examination, general appearance is crucial. Hypoxemia (Table 2).

In laboratory findings, WBC and CRP are main items.

Regarding physiology of COPD, most important tool for diagnosis of COPD is pulmonary function test (PFT). Key issue is under 0.70 of ratio of forced expiratory volume in one second (FEV1) forced vital capacity (FVC). Next step is evaluation of severity. It is based on the Global Initiative for chronic obstructive pulmonary disease (GOLD) staging. They propose four stages according to the percent predicted FEV1. All these values are obtained after bronchodilator. Bronchodilator. And inspiratory capacity (IC) is crucial surrogate index for severity of air-trapping. In management point of view, long acting bronchodilator is effective for increase of IC. Besides, if ratio of IC/total lung capacity (TLC) is under 25%, it predicts poor prognosis. Needle to say, body weight loss also have relationship with worse prognosis.

In laboratory findings, there are some reports that fibrinogen and surfactant protein D (SP-D) are associated with acute exacerbation of COPD.

Third, I describe approach for bronchial asthma. On history taking, cardinal symptoms are wheezy dyspnea, cough and chest tightness. In terms of asthma on set, age of 12 is important. Before 12, childhood asthma is likely and usually associated with atopy and environmental factors. After 12, adult on set asthma is possible, obesity and chronic sinusitis contribute (Table 3).

In terms of physical examination, orthopnea is significant in asthma attack. Jugular vein show variable dilatation accompanied with respiration.

In short, jugular vein show more distention in expiratory phase. On the other hand, jugular vein show more collapse in inspiratory phase. Lung auscultation of asthma patients typically show distant or early crackles, and early-to-mid inspiratory crackles. These sound correspond to hyperinflation, severe air-trapping and chronic inflammation of more central airways. In peripheral muscle, pigmentation of distal part of quadriceps muscles is called thinker’s sign and this means chronic lean forward posture of patients. Facial and leg edema is associated with cor pulmonale or chronic hypercapnia. Hypercapnia play a role for absorption of free water accompanied with bicarbonate from proximal renal tubule. In addition, ankle edema have relationship with pulmonary hypertension (PH) especially in COPD patients.

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In short, jugular vein show more distention in expiratory phase. On the other hand, jugular vein show more collapse in inspiratory phase. Lung auscultation of asthma patients typically show phoncic wheezes expiratory or both phases. In status asthmatics, auscultation demonstrates silent because of severe air flow limitation. In extremities, edema is absent and this is important differential point from congestive heart failure.

Regarding physiology of asthma, one of the important item is airway reversibility in PFT. However, over half of the COPD patients also show reversibility. Therefore, comprehensive approach is crucial for secure diagnosis of asthma.

In laboratory findings, evaluation of absolute value of peripheral eosinophil and IgE are important for allergic status. If significant eosinophilia or marked elevation of IgE is identified, we should consider allergic broncho-pulmonary aspergillosis (ABPA) or eosinophilic granulomatosis with polyangiitis (EGPA). Exhaled nitric oxide (eNO) is useful marker of eosinophilic airway inflammation. However, over 35 ppm of eNO, inhaled corticosteroid (ICS) is recommended to relief eosinophilic airway inflammation. Smoking usually decrease the value of eNO.

Finally, I describe approach for interstitial lung disease (ILD). On history taking, progressive exertional dyspnea and non-productive cough are main symptoms. Modified medical research council (mMRC) breathlessness scale are often used for evaluation of chronic
In heart examination, elevation of S2 and pansystolic murmur at parasternal area suggest PH. If accentuation of pansystolic murmur is reproduced when inspiratory phase, tricuspid valve regurgitant murmur is most likely. In addition, parasternal lift is confirmed, the patient’s systolic pulmonary arterial pressure (PAP) may be over 50mmHg.

In extremities, clubbing is most crucial finding which means chronicity of lung disease. Among the diffuse lung diseases, idiopathic pulmonary fibrosis (IPF) and Rheumatoid arthritis (RA) associated ILD more often show clubbing [31]. COPD and tuberculosis (TB) rarely have clubbing. In addition, heliotrope rash and Gottron’s sign are carefull findings. Because these findings with ILD suggest amyopathic dermatomyositis (ADM) associated ILD which often have relentless course such as progressive respiratory failure [32]. On the contrary, mechanic hand and proximal muscle ache are associated with anti-Aminoacyl tRNA synthetase (Anti-ARS) syndrome which usually show good response to systemic steroid and good survival [33]. Therefore, detection of specific findings in ILD patients is important for management and prediction of clinical course. And if we see palpable puple and systemic symptoms such as fever, vasculitis such as Myeloperoxidase Anti-neutrophil cytoplasmic antibody (MPO-ANCA) associated disease is possible.

Physiological point of view, FVC is most important surrogate marker for prediction of clinical course in ILD [34]. Over 10% decline of percent FVC (%FVC) within one year is related with worse survival. In IPF patients, over 5% decline of %FVC within three months predicts of short-term mortality [35]. Diffusing capacity of the lung for carbon monoxide (DLco) is rather sensitive parameter of activity of ILD especially early phase. And over 15% decline of percent DLco (%DLco) is associated with poor prognosis. (Table 4) However, if vital capacity of patient is less than 1500ml, we usually cannot evaluate DLco precisely in single breath method. And DLco is sometimes affected by respiratory infection. Therefore, FVC is more reproducible, reliable and robust physiological marker than DLco. When we see combined pulmonary fibrosis and emphysema (CPFE) patients, FVC are preserved [36]. Therefore, I recommend to use composite physiological index (CPI) when we evaluate disease activity of CPFE [37]. Besides, DLco/alveolar volume (KCO) is useful indicator. Over 15% decline of KCO is important threshold for PH prediction [38]. In systemic sclerosis (SSc) associated ILD patients, %FVC/%DLco over 1.6 means existence of PH [39].

6 minute walking test distance (6MWTD) is classic useful physiological test for chronic lung disease. In IPF patients, over 25 m decline of 6MWTD within 6 months predicts short-term mortality [40]. And heart rate recovery after one minute (HRR1) after 6MWT is crucial parameter. If less than 13 of HRR1 is associated with poor prognosis of ILD [41].

In laboratory findings, Krebs von den Lungen-6 (KL-6) and surfactant protein D (SP-D) are most useful biomarker for ILD. KL-6 is sensitive for prediction of disease activity and usually associated with extent of fibrosis. And over > 1000 is related with acute exacerbation (AE) of CPFE [42]. And if seasonal variation of KL-6 is shown, chronic hypersensitivity pneumonitis (CHP) is possible [43]. Marked elevation of KL-6 is associated with NSIP, CHP and pulmonary alveolar proteinosis (PAP) [44]. On the other hand, SP-D is sensitive marker of more acute or subacute ILD such as acute eosinophilic pneumonia (AEP) and organizing pneumonia (OP). And SP-D have negative associated with VC and positive relationship with ground glass opacity (GGO) in high resolution computed tomography (HRCT) of the chest [45].

In conclusion, approach for respiratory diseases require both clinical and physiological viewpoints. It will lead to adequate evaluation of imaging and pathology.

**CONFLICT OF INTERESTS**

The author has no conflicts of interest to declare.

**REFERENCES**

12. Bettoncelli G. Errata Corrig: The clinical and integrated man-
agreement of COPD. Sarcoïdosis Vasc Diffuse Lung Dis 2014; 3(2):3753.


