SCLERODERMA SPECTRUM: PULMONARY COMPLICATIONS

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Scleroderma – Hard skin
SSc & scleroderma-spectrum disorders

- No diagnostic test for scleroderma
- Pathogenesis is unknown
- Prominent features of disease reflect characteristic pathophysiologic triad of autoimmunity, inflammation, vascular damage & fibrosis
- Affects 1 in 4000 adults in USA; 120,000 cases
- Female predominance
- More severe in African-Americans than Caucasians
- Has the highest case-fatality among CTD with a 10 year survival of 55%

Limited and Diffuse SSc—Skin Involvement

Limited

Diffuse
CLASSIFICATION:

- Diffuse cutaneous
- Limited cutaneous
- Overlap or mixed connective tissue disease (MCTD)
- Myositis (dermatomyositis and polymyositis)
Clinical manifestations related to fibrotic and vascular disease:

- Heart
- Lung
- GI tract
- Kidney
- Skin- digital ischemia; contractures of oral structures making intubation difficult

**Skin Thickness in Scleroderma**

**Scleroderma spectrum-organ involvement**

Figure 3.2. Diagrammatic representation of the stages of diffuse and limited scleroderma over time, including the typical relationships between skin thickness and selected organ system involvements.
Masson-Trichrome stain of a digital artery from a patient with diffuse scleroderma
**Lung complications in SSc spectrum**

- ILD • Nonspecific interstitial pneumonia (NSIP) • Usual interstitial pneumonia (UIP)
- Diffuse alveolar damage (DAD)
- Cryptogenic organizing pneumonia (COP)
- Pulmonary hypertension
- Pleural involvement
- Aspiration pneumonia
- Alveolar hemorrhage
- Small airways disease
- Malignancy
- Respiratory muscle weakness
- Drug-induced toxicity
- Spontaneous pneumothorax
- Pneumoconiosis (silicosis)

**Scleroderma Lung Disease**

- Alveolitis
- Interstitial fibrosis
- Recurrent aspiration
- Pulmonary vasculopathy

The major clinical issue is defining the relative contribution of each process and choosing appropriate therapy.
Key tests in ILD monitoring

- Pulmonary function test with DLCO
  -- Presence of ILD causes reduced lung volumes or restrictive lung disease: < %FVC and < %TLC
  --- reproducible
  --- progression of lung disease variable & difficult to predict

- High Resolution CT scan chest
- Echo/doppler study

Hematoxylin and eosin stain of lung from patient with fatal interstitial lung disease. There is interstitial fibrosis, persistent interstitial inflammation, and striking intimal hyperplasia of a pulmonary arteriole.
Interstitial pneumonia termed centrilobular fibrosis (CLF), characterized by a prevalent bronchocentric distribution of lesions, bronchi containing intraluminal foreign bodies, and basophilic matter with occasional multinucleated giant cells. This underappreciated pattern of ILD has been causally linked to chronic aspiration.

De Souza -- various clinical, histopathologic, and radiological attributes were found to support the link between aspiration and the development of SSc-ILD.

Carvalho et al: *Pathol Res Pract* **198** (9)
High resolution CT of lung in patient with early SSc. Note Scattered “ground glass” appearance of bibasilar alveolitis

Interstitial Lung Disease

- Occurs in both: limited (23%) vs diffuse SSC (>40%)
- Prevalence 20-90% depending on method of dx
- PFT: restrictive pattern
- Most frequent: NSIP (78%)*
- High Resolution chest CT: ILD found in 90-100%

Predictors of increased risk of SSc-related ILD

_but do NOT predict severity_

- Anti-topoisomerase (Scl-70)
- Nucleolar auto-antibody (+ ANA by IFA)
- Anti-Th/T0
- Anti-U3 RNP
- African Americans
- Other organ involvement (heart, muscle, renal)
- High skin scores

Hematoxylin and eosin stain of lung from patient with fatal interstitial lung disease. There is interstitial fibrosis, persistent interstitial inflammation, and striking intimal hyperplasia of a pulmonary arteriole.
Scleroderma-related PAH

- SSc-related PH leading cause of death –
- If untreated- PAH causes RV hypertrophy, RV pressure overload, dilation and death due to RV failure
- Integrity of RV function rather than degree of vascular disease that determines symptoms and mortality

Pulmonary HTN screening

- Pulmonary hypertension (PH) can be suggested by echo but must be confirmed by right heart cath.
- PFT- show diminished %DLCO disproportionately to %FVC (ie: FVC/DLCO >1.6)
- echo/doppler >50 mm Hg
- 6-minute walk test (measure oxygen saturation, distance; dyspnea index)
- Right heart catheterization (mean PA, CO, CI, PCW)
PAH definition:

The definition of PH, as follows:

- The proposed new definition of PH is a resting mPAP $\geq 25$ mm Hg.
- The exercise and PVR criteria should be eliminated.
- A resting mPAP of 8 to 20 mm Hg should be considered normal, based on available evidence.
- Further studies are needed to better determine the natural history of patients with mPAP 21 to 24 mm Hg.

Badesch et al JACC 2009: S55-66)

PAH classification- Dana Point 2009

- **WHO Group I**: increased PVR due to vascular remodeling and occlusion of pulmonary arteries: SSc-PAH is in this group
- **WHO Group II**: PH due to left sided heart disease: including diastolic dysfunction.
- **WHO Group III**: due to lung disease (ILD) and chronic hypoxia
- **WHO Group IV**: chronic thromboembolic dz
- **WHO Group V**: unclear etiology/miscellaneous
Survival in Scleroderma Patients with PH, Lung Involvement, or No Major Organ Involvement

PH management:

- **PDE-5 inhibitors**: sildenafil, tadalafil
- **ERB**: bosentan, ambrisentan, *(in clinical trial: sitaxsentan, etc)*
- **Prostacyclins**: epoprostenol (IV) treprostinil: IV, SQ, inhaled, *(oral in trial)* iloprost (inhaled; *IV available in Europe*)
- **Lung transplantation**
**Clinical differences between idiopathic and scleroderma-related pulmonary hypertension**

![Graph showing percent survival over time for idiopathic pulmonary arterial hypertension (IPAH) and pulmonary arterial hypertension associated with scleroderma (PAH-Scl)](image)

*Arthritis & Rheumatism, Volume 54, Issue 9, pages 3043-3050, 31 AUG 2006*

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**PH Registries:**

- **REVEAL**  Registry to Evaluate Early and Long-term Pulmonary Arterial Hypertension Disease Management

- **PHAROS**  Pulmonary Hypertension Assessment and Recognition of Outcomes in Scleroderma

- **UK CTD-APAH registry**
## Challenges in ICU management of SSc

<table>
<thead>
<tr>
<th>Condition</th>
<th>Diagnosis/Procedure</th>
<th>Management/Notes</th>
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</thead>
<tbody>
<tr>
<td>Tamponade</td>
<td>echo/RHC</td>
<td>short trial of steroid, needle drain/window</td>
</tr>
<tr>
<td>RHF</td>
<td>RHC for dx</td>
<td>IV prostacyclin, diuretics, oxygen, notropes</td>
</tr>
<tr>
<td>Flare of ILD</td>
<td>HRCT, nl PCW</td>
<td>lung bx- lung transplantation; treat CHF/infections; no role for steroid</td>
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<tr>
<td>Renal crisis</td>
<td>triad present</td>
<td>short acting ACE- oral captopril, enalapril until DBP &lt;80 and SBP &lt;120; continue ACE if dialysis occur for 6-12 months</td>
</tr>
<tr>
<td>Digital ischemia</td>
<td>angiogram</td>
<td>IV prostacyclin; digital block</td>
</tr>
<tr>
<td>Bowel obstruction</td>
<td>CT Abd</td>
<td>decompress with NGT/rectal tube; TPN; prokinetic agents</td>
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Farber et al: *J intensive Care Med: June 2010 (10):1-12*