Respiratory Disorders in MARFAN SYNDROME

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Shortness of Breath in MFS: Three Possibilities

HEART
- Valvular heart disease
- Arrhythmias
- Cardiomyopathy

LUNGS
- Chest wall deformities
- Respiratory Muscle Weakness
- Enlarged airspaces (emphysema)
- Pneumothorax
- Sleep apnea syndrome
- Asthma
- Pulmonary hypertension

DECONDITIONING
Why are there lung problems in MFS?

Fibrillin-1 is expressed in the lung. Fibrillin-1 is associated with elastin and connective tissue.

• Candidate diseases
  – Emphysema (elastin/developmental)
  – Pneumothorax (elastin/developmental)
  – Sleep apnea (connective tissue)
  – Lung musculoskeletal impairment (connective tissue)
Restrictive Lung Disease

• >50% of pts with Marfan Syndrome
• Musculoskeletal abnormalities of the chest
• Cannot expand the chest fully
• Symptoms:
  – Shortness of breath with exertion
  – Cyanosis, Heart strain
Spirometry
Pulmonary Function Testing (PFTs)
Restrictive Lung Disease - Lung Function

Reduction in Lung Capacity!
Skeletal Abnormalities and Restrictive Lung Disease - MFS

Scoliosis

Respiratory Muscle Weakness

Pectus Abnormality
Neuromuscular disorders and Restrictive Lung Disease

• Marfan Syndrome can be associated with skeletal muscle weakness.
• Weak respiratory muscles can lead to reduced lung capacity → Restriction
• Diagnosis: Pulmonary Function Tests which include Maximal Inspiratory and Expiratory Pressures.
• Treatment: Pulmonary Rehabilitation, Ventilatory Support
Pectus Abnormalities

Pectus Excavatum

Pectus Carinatum

Present in two-thirds of patients with Marfan Syndrome
Natural History
Pectus Abnormalities

• Typically benign, but few studies. Modest reduction in lung function.

• Evidence or potential for respiratory dysfunction is often the stated reason for early repair of severe defects, although **cosmesis is typically of greater concern**.
Treatment of Pectus Abnormalities

NUSS PROCEDURE

Advantages
-- Easier
-- Shorter
-- Fewer complications
-- 21 yr f/u—good anatomic result, limited lung function data
Does correction of pectus deformities improve lung function?

Probably NO.

Considerations:

-- Complexity of chest wall defects, esp. if associated with scoliosis in persons with Marfan Syndrome may lead to more accelerated lung dysfunction without repair.

-- Need for assessments of functional capacity: six minute walk tests, cardiopulmonary exercise testing.
KyphoScoliosis-Factors Predisposing to Respiratory Insufficiency

- Cobb Angle >100°
- Age of Onset
- Sleep-Related Abnormalities
- Underlying etiology
- Inspiratory Muscle Weakness

Modified from Fishman’s Pulmonary Diseases and Disorders. 1999.
VC (% pred) = 87.6 - 0.338 X Cobb Angle
Thoracic curves worse than thoracolumbar curves!
# Restrictive Lung Disease - Scoliosis Severity

<table>
<thead>
<tr>
<th>Cobb Angle</th>
<th>Clinical Manifestations</th>
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<tbody>
<tr>
<td>&lt;10°</td>
<td>Normal, no symptoms</td>
</tr>
<tr>
<td>&gt;25°</td>
<td>Incr. pulmonary vascular pressures, no symptoms</td>
</tr>
<tr>
<td>&gt;40°</td>
<td>Consider surgical intervention</td>
</tr>
<tr>
<td>&gt;70°</td>
<td>Reduced lung volumes</td>
</tr>
<tr>
<td>&gt;100°</td>
<td>Shortness of breath with activity</td>
</tr>
<tr>
<td>&gt;120°</td>
<td>Chronic respiratory failure, oxygen supplementation, non-invasive ventilation</td>
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Koumbourlis, 2006 Pediatric Respiratory Reviews
Scoliosis - Pulmonary Evaluation

Full PFTs (pulmonary function tests), with DLCO, MIP/MEP

SNIFF Fluoroscopy to assess diaphragmatic function

Six minute walk test

+/− Sleep study
Scoliosis-Treatments

**Observation**
- q6months examination
- q12months spinal films

**Cast/Bracing**
- Milwaukee Brace with superstructure
- Charleston Night time side bending orthosis
- TLSO Low profile orthosis

**Surgery**
- Rod placement +/− fusion
- Growing rod placement
- VEPTR
- Spine staples
- Magnetic rods (MCGRs)
Scoliosis-Treatments

Dual Goals of Intervention:
Prevent further structural deformity
Preserve or improve pulmonary function

**BRACING**
Progressive curvature <45°.

**SURGERY**
Progressive curvature despite bracing.
Cobb angle >70°
Respiratory failure
Restrictive Lung Disease-MFS

• **Pectus Deformities**
  – Surgical repair does not correct restriction.
  – Cosmesis should dictate repair unless severe deformity.

• **Scoliosis**
  – Typically corrected early.
  – Progressive curvature without correction.
  – Pulmonary consequences without correction of severe thoracic deformity probably significant.

• **Neuromuscular Dz**
  – Pulmonary Rehabilitation
  – Ventilation strategies
1. **Noninvasive Positive Pressure Ventilation** — May improve survival in selected pts; may improve dyspnea in less severe dz.

2. **Pulmonary Rehabilitation** — Improves lung volumes and exercise capacity. **?Role preop.**

3. **Supplemental Oxygen** — If desaturation at rest or with activity

4. **Bronchodilators** if air trapping or wheezing.

5. **+/- Airway clearance devices**, Flutter valve
Restrictive Lung Disease-MFS

Take Home Messages

• Need serial pulmonary function tests to follow progression of pulmonary restriction. Functional assessment of value.

• Appropriate surgical intervention for scoliosis may prevent or delay further deterioration in lung function.

• Pectus repair should be driven by cosmesis unless complex chest wall deformity or significantly reduced lung function.
Marfan Syndrome and Pneumothorax

• What is pneumothorax?
  – “Lung collapse”; lung detaches from chest wall.

• What are the symptoms?
  – Acute onset of pleuritic chest pain, shortness of breath and dry cough.

• How is it diagnosed?
  – Chest Xray
  – CT Scan
Pneumothorax
18 yo man with MFS and recurrent bilateral pneumothoraces

Apical blebs
Pneumothorax--Treatment

- If small, hospitalization & supplemental oxygen.
- If moderate→large, chest tube placement for evacuation.
- If unresponsive to above or recurrent, pleurodesis is indicated. Mechanical better than chemical pleurodesis.
- Alternative to chest tube, Heimlich valve
Thoracoscopy
Pneumothorax - *Indications for Surgery*

*(Bleb resection and mechanical pleurodesis)*

- Massive air leak, poor re-expansion
- Recurrent pneumothorax
- Persistent air leak 7-10 days
- Simultaneous bilateral
- Hemopneumothorax
- Tension pneumothorax
- Large blebs/cysts
Pneumothorax--MFS

Take-Home Messages

- Pneumothorax is a common manifestation of Marfan Syndrome.
- If recurrent, pulmonary consultation should be obtained.
- Efforts at durable reexpansion should observe surgical considerations of eventual aortic repair. Mechanical pleurodesis preferred.
Emphysema in Marfan Syndrome

What is emphysema?
--Loss of alveolar walls (genetic and/or destructive)
--Enlargement of airspaces
--Airway obstruction/inflammation
Emphysema Findings—
Fewer alveoli
Irreversible
Emphysema--Symptoms

• Shortness of breath with activity
• Frequent bouts of “bronchitis”
  – Cough with green sputum
  – Chest congestion
  – After common cold or viral infection
• Low blood oxygen
Emphysema--Diagnosis

- Chest X-Ray
- Chest CT Scan, high resolution scan
- Pulmonary Function Tests
- Arterial Blood Gas
Emphysema--Treatment

• Conventional
  – Bronchodilators
  – Inhaled Steroids
  – Oxygen, if necessary
  – Aggressive treatment of infections
  – Lung volume reduction surgery

• Experimental
  – Retinoic acid
  – Cytokine inhibition (Losartan)
  – Antioxidants
Emphysema--MFS

Take-Home Messages

• Emphysema is probably a sequelae of disturbances in lung development in Marfan patients.

• Symptoms of shortness of breath, recurrent bronchitis, pneumothorax should prompt evaluation by a lung specialist for emphysema and initiation of treatment.
Sleep Apnea

- Defn: Intermittent cessation of airflow at the nose and mouth during sleep.
- Affects ~2% middle-aged women, 4% middle aged men.
- Cause of excessive daytime sleepiness
- Obstructive—Can’t breathe
- Central—Won’t breathe
**Normal Breathing**

- Air flow
- Tongue
- The roof of the mouth
- Tonsils

**Sleep Apnea**

- Air flow
- Breathing blocked

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**Figure 3**
Sleep Apnea

- Common in general population (>15 million Americans)
- Potentially life-threatening w/ high clinical impact
  - Motor Vehicle Accidents
  - Arrhythmias, heart attacks, aortic dissection
  - Strokes
  - Reduced Productivity
  - Reduced quality of life
Nature of the Problem

• Recent studies have shown that up to 35% of patients with MFS have sleep apnea. (Control population-<5%)

Marfan Syndrome (Fibrillin-1 deficiency)

• Craniofacial Dysmorphology
  • Floppy upper airways
  • Chest wall abnormalities

• SLEEP-DISORDERED BREATHING
  • --Obstructive sleep apnea
  • --Central sleep apnea
Sleep Apnea-Aorta Connection

Proposed Paradigm

MFS

Obstructive Sleep Apnea

Aortic Enlargement

Intrathoracic pressure changes
Systemic HTN
Hypoxia, Oxidative Stress, Inflammation

Progression

OSA Treatment

Aortic Rupture

Aortic Dissection
Sleep Apnea in Marfan Syndrome

• Diagnosis:
  – Sleep Study
    • Brain activity, eye movements, muscle activity, airflow, oxygen levels
    • Awakenings—Apnea/hypopnea index, Abnl >5
    • Sleep latency—Abnl <5 minutes
  – Measurement of upper airway resistance during sleep
Sleep Apnea in Marfan Syndrome

Treatment

– Nasal CPAP
– +/- Supplemental oxygen
– If difficulty with CPAP mask fitting, consider
  • Mandibular advancement device
  • Oral appliance
– +/- Weight loss
– Drugs—Strong central component
– Rare—Surgery (uvulopalatoplasty, tracheostomy)
How does Nasal CPAP work?
Sleep Apnea Devices

- Apnea Pillows
- Nasal Mask
- Full Face Mask
- Dental Device
Sleep Apnea in Marfan Syndrome

Take-Home Messages

• Underdiagnosed in Marfan Syndrome

• All adult patients with Marfan Syndrome should be considered for screening, especially if sleep disturbances or severe chest wall deformity.