



BRIGHAM AND  
WOMEN'S HOSPITAL

| The Lung Center |

# Asthma mimics: Consider tracheobronchomalacia



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HARVARD MEDICAL SCHOOL  
TEACHING HOSPITAL

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# Disclosures

- Dr. El Boueiz:
  - Educational Speaker, Chiesi
  - Educational Speaker, Thorasys Thoracic Medical Systems
- Dr. Shafiq:
  - Consultant, Ambu A/S



# Case example - 38F with asthma symptoms

- Current symptoms began after 3<sup>rd</sup> childbirth
- History:
  - Asthma:
    - Frequent hospitalizations for SOB and wheezing
    - Intubation and mechanical ventilation (brief)
    - Triggers: Respiratory tract infections
    - Allergy testing: Positive for dust mites
    - Maintained on LABA/ICS
  - BMI: 45
  - 10 pack-year smoking history (quit 10 years ago)
  - Homemaker with 2 Golden Retrievers
- Clinical findings:
  - Diffuse expiratory wheezing and non-productive cough

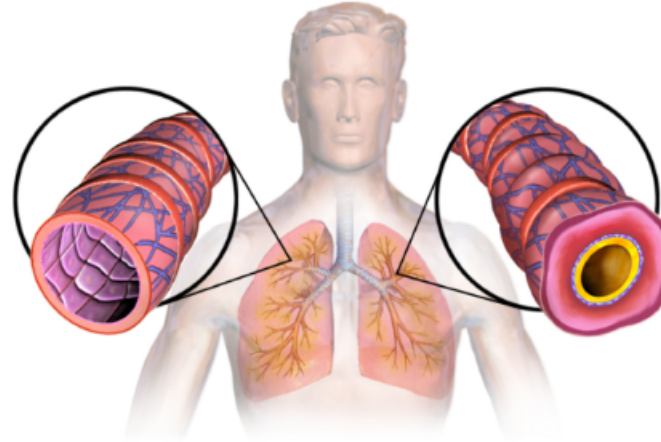


# Case example – Continued

- Persistent symptoms despite treatment.
  - Current treatments:
    - Anti-IgE monoclonal antibody and low-dose daily steroids
  - Key symptoms:
    - Loud, persistent cough
    - Difficulty clearing chest secretions
    - Daily wheezing
    - Marked DOE
  - Clinical findings:
    - Normal vital signs (SpO<sub>2</sub> 96% on room air at rest)
    - Intermittent diffuse expiratory wheezes audible without stethoscope
    - Loud cough
  - Diagnostics:
    - Variable PFTs: mild restriction or mild airflow obstruction
    - Normal indirect laryngoscopy



# Asthma Mimics

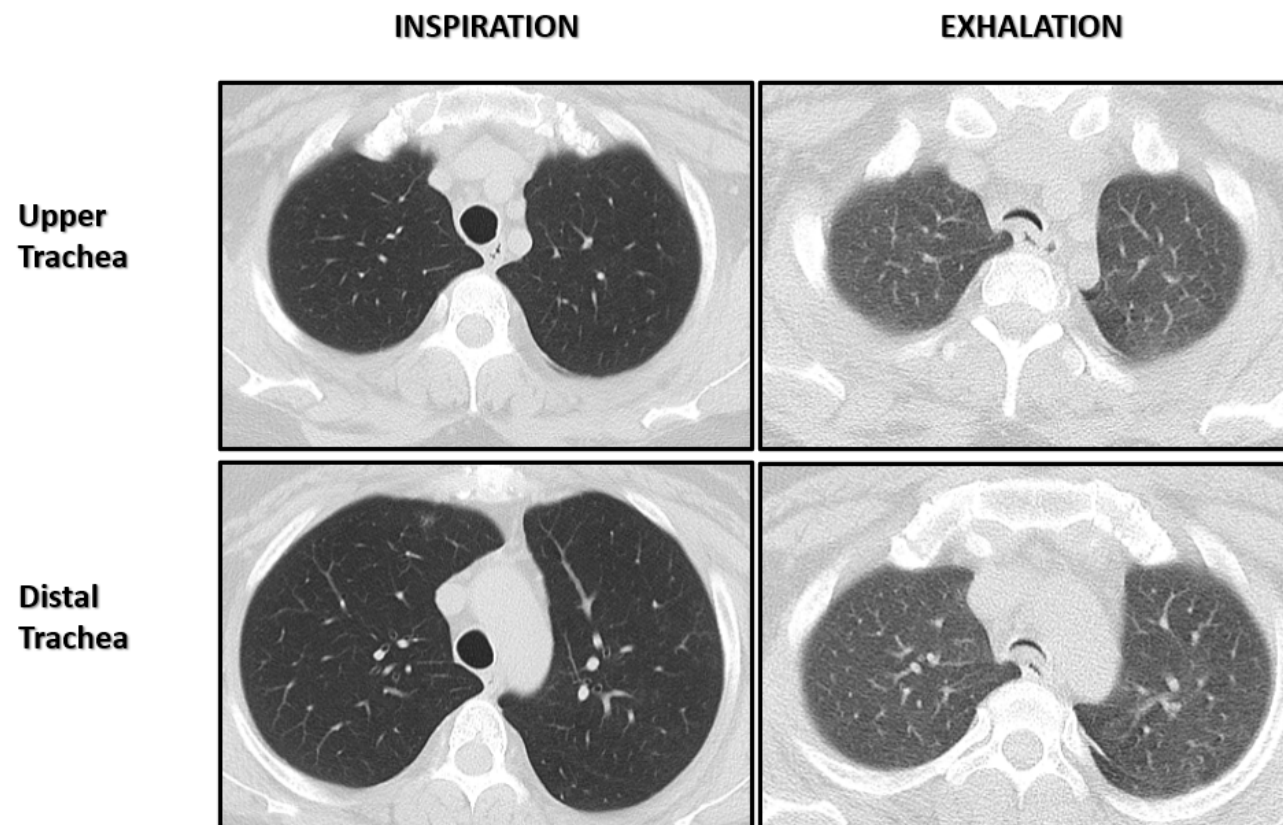


- Upper airway:
  - Vocal cord dysfunction
  - Tracheal tumor / stricture
  - Foreign body aspiration
  - Vascular sling
- Lower airway:
  - COPD
  - Bronchiectasis
  - Constrictive bronchiolitis

- Other:
  - Heart failure
  - Sarcoidosis
  - Eosinophilic bronchitis
  - Pulmonary embolism
  - LAM
  - Disseminated strongyloidiasis

... and consider TBM

# Case example – Continued - Dynamic CT chest



> 50% luminal narrowing of the trachea during expiration

# Outline –

## *Asthma mimics: Consider tracheobronchomalacia*

- Definition
- Etiology / Risk factors
- Clinical manifestations
- Evaluation
- Treatment options



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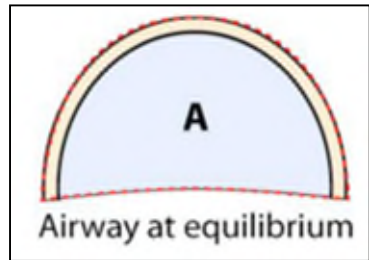


# Tracheal collapse

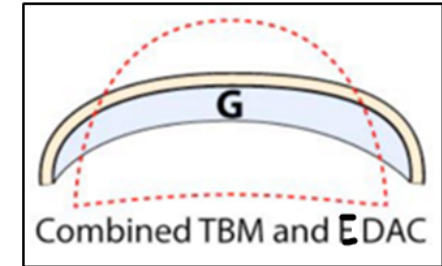
- Dynamic Central Airway Obstruction:
  - Luminal narrowing < 50% during expiration
- Tracheomalacia (TM) or Tracheobronchomalacia (TBM):
  - In Greek, “malakia” = softness → TM / TBM: Cartilage weakness / softening of the trachea and/or mainstem or lobar bronchi
  - Cartilage injury makes airways prone to pressure changes, causing collapse on exhalation and expansion on inhalation.
- Excessive Dynamic Airway Collapse (EDAC):
  - Excessive laxity of the posterior membranous wall with intact cartilage support
  - Bulging of the posterior membrane into the airway lumen during exhalation
- Excessive central airway collapse (ECAC):
  - Imaging and bronchoscopy often cannot distinguish the relative contributions of TBM, EDAC, or both to airway narrowing

Chest 2005;127(3):984-1005 // Treat Respir Med 2006;5(2):103-115

# Classification of collapse



DAC	Physiologic CSA narrowing	 Forced expiration
EDAC	Pathologic bulging of posterior membrane	
Crescent-type TBM	Anterior cartilage softening	
Saber-sheath TBM	Lateral cartilage wall softening	
Circumferential TBM	Both anterior and lateral wall collapse	



Respirology 2006;11(4):388-406

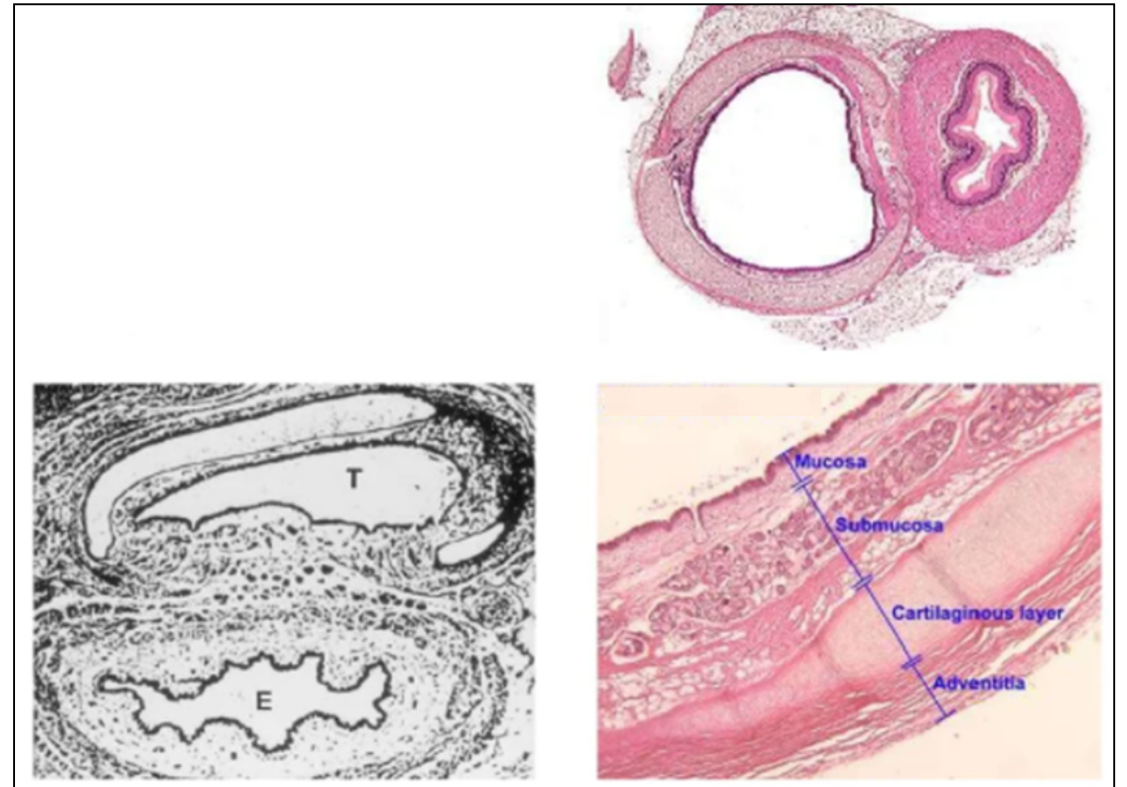
# Optimal diagnostic threshold for luminal narrowing?

- No universally accepted cut-off value to define normal and abnormal airway narrowing.
- Defined by at least 50% decrease in the area from inspiration to expiration.
  - If forced expiration, cutoff is 70%
  - No clear cutoff for bronchial collapse
  - Accepted by convention, but may not be true, and ~80% of normal individuals exceed the current diagnostic criterion
- What to measure ???!!!
  - Degree of collapse (50% reduction? By diameter or cross-sectional area (CSA)?)
- When do we measure it ???!!!
  - During tidal breathing
  - During forced expiration
  - During coughing

Radiology 2009;252(1);255-262  
Clin Chest Med 2013;34:527-555

# Histopathology

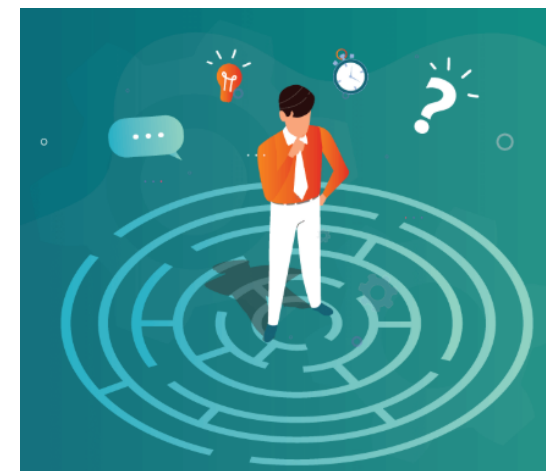
- Atrophy of the longitudinal elastic fibers
- Fragmentation of the tracheal cartilage
- Tracheal cartilage-to-soft tissue ratio:
  - Normal: ~ 4.5:1
  - In TBM: Often as low as 2:1
- TBM may result from a fibrotic process with increased Collagens I and III but not IV, similar to pulmonary fibrosis.
  - Mechanism is unclear but may involve epithelial mesenchymal transition



Courtesy: University of Illinois Medical Center

J Thorac Imaging 2011;26(4):278-89

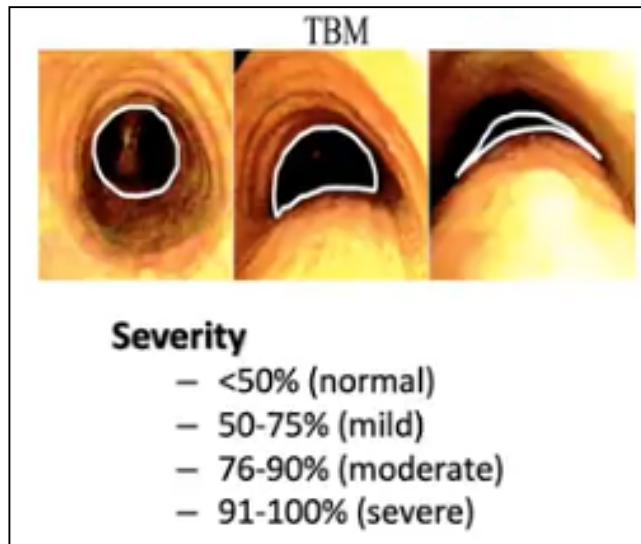
# Challenges in clinical understanding



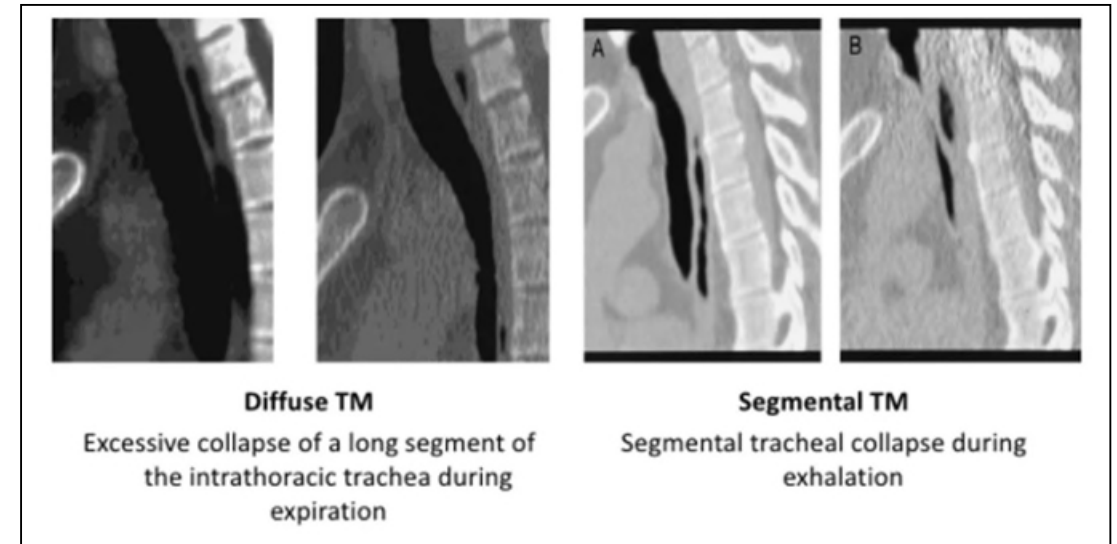
- Prevalence and natural history:
  - Uncertainty about prevalence in asymptomatic vs. symptomatic populations
    - *Biased sampling of smokers, older adults, and those with lung diseases*
  - Limited data on progression and outcomes without treatment
- Symptom attribution:
  - Debate over whether TBM/EDAC is a primary condition or secondary to other diseases (e.g., asthma, COPD, GERD)
  - Debate over whether symptoms like dyspnea, cough, and wheezing are solely due to TBM/EDAC or coexisting conditions (e.g., asthma, COPD, GERD)
- Clinical impact:
  - Disagreement on the extent to which TBM/EDAC impacts QoL and long-term outcomes
  - Difficulty distinguishing clinically significant cases from incidental findings

# Classification by severity and distribution

## Severity



## Distribution



Chest 2005;127:984-1005 // Chest 2007;131:1118-1124 // Chest 2007;132:609-616 // Radiology 2009;252:255-262 // Radiology 2010;257(2):560 // Chest 2012;142(1):168-174

# FEMOS classification

- **FEMOS:**
  - **Functional class:**
    - NYHA I-IV
  - **Etiology:**
    - Primary, secondary
  - **Morphology:**
    - Saber sheath, crescentic, circumferential ...
  - **Origin:**
    - TM, BM, TBM (focal/multifocal/diffuse)
  - **Severity:**
    - Mild, moderate, severe

Respirology 2006;11(4):388-406

# Outline –

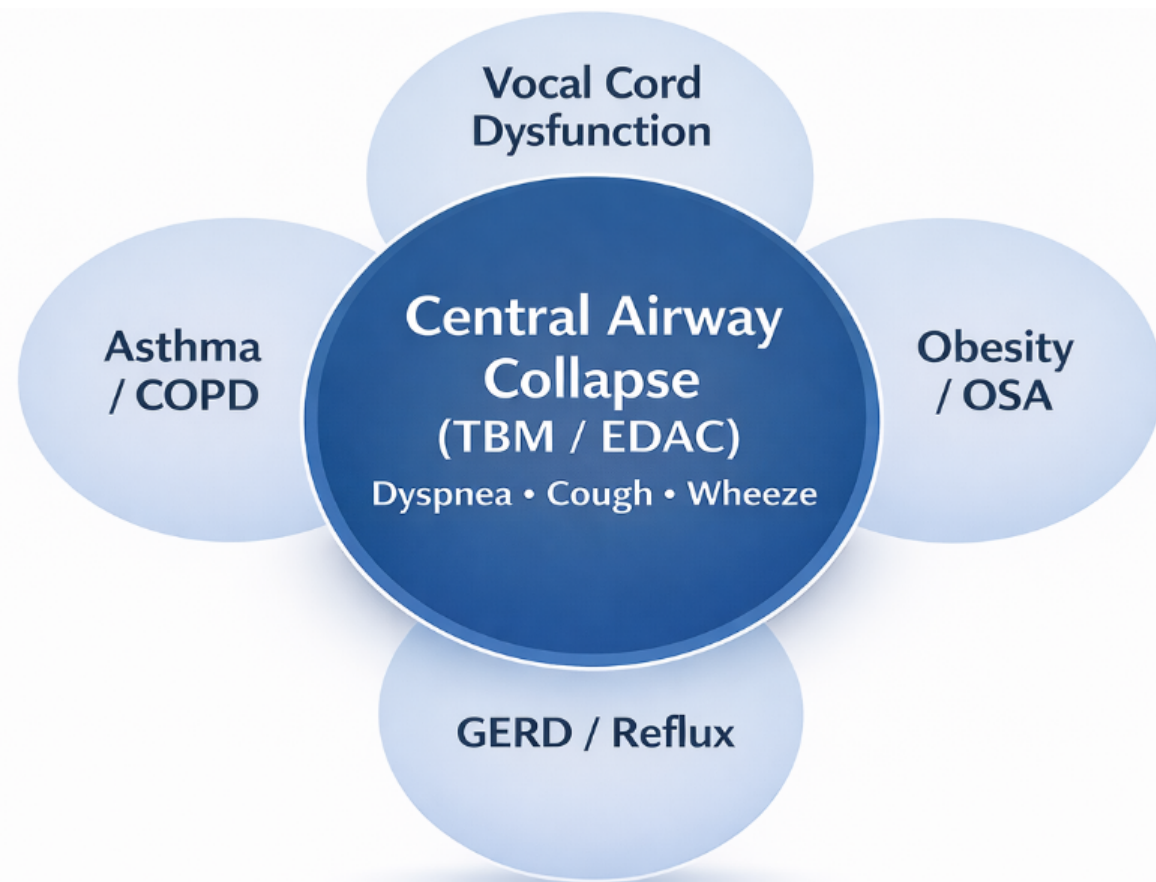
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# Clinical conditions that overlap with TBM / EDAC

- TBM frequently coexists with conditions that produce similar symptoms such as dyspnea, cough, and wheezing.
- Recognizing these overlapping disorders is essential for accurate diagnosis and appropriate management.



# Etiology

<b>Primary or Congenital</b>
Genetic, such as polychondritis (See also Pediatric table)
Idiopathic "Giant Trachea" or Mounier-Kuhn
<b>Secondary or Acquired</b>
Post-traumatic
Post intubation
Post tracheostomy
External chest trauma
Post lung transplantation
Emphysema
Chronic Infection/Bronchitis
Chronic Inflammation
Relapsing Polychondritis
Chronic External Compression of the Trachea
Malignancy
Benign Tumors
Cysts
Abscesses
Aortic aneurysm
Vascular Rings, previously undiagnosed in childhood

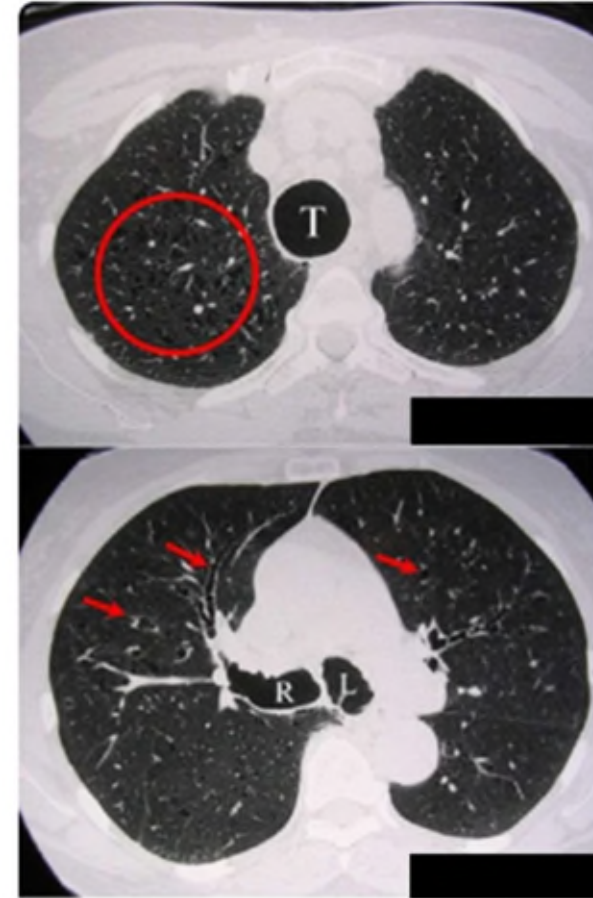
Respirology 2006;11(4):388-406

# Etiology

- Localized:
  - Prolonged intubation / tracheostomy
  - Vascular sling
  - Resection of anterior mediastinal mass
- Diffuse:
  - COPD (saber-sheath trachea)
  - Tracheomegaly
  - Ehlers-Danlos syndrome
  - EDAC:
    - ? Inhaled steroids
    - ? Obesity
    - ? Smoking
- Diffuse tracheal wall thickening, sparing the posterior membrane:
  - Relapsing polychondritis
  - Tracheobronchopathia osteochondroplastica
- Diffuse circumferential tracheal wall thickening:
  - Sarcoidosis
  - Granulomatosis with polyangiitis (GPA)
  - Amyloidosis
  - Inflammatory bowel disease

# Tracheobronchomegaly - Mounier-Kuhn syndrome

- 3<sup>rd</sup> or 4<sup>th</sup> decade of life
- Atrophy of longitudinal elastic fibers and thinning of the muscularis mucosa
- Diagnostic criteria:
  - Right mainstem > 2.4 cm
  - Left mainstem > 2.3 cm
  - Trachea exceed > 3 cm
- Chronic accumulation of secretions
  - Recurrent infections
  - Bronchiectasis
  - Rarely pulmonary fibrosis



Br J Radiol. 1984;57(679):640-644

# Relapsing polychondritis

- Inflammatory condition affecting cartilage across the body
- Cellular and humoral response against collagen type II, IX, and XI (30-70% of patients)
- Involves tracheal rings in 56% of cases, but respiratory symptoms on presentation in only 14% of cases:
  - Sparing of the posterior wall
  - Smooth, long-segment involvement
  - May calcify (typically thick)
  - Worse prognosis and poorer response to steroids (5-year survival rate: 45-74%)
- Delay in diagnosis ~ 3 years; Asthma mimic. When suspected, look for:
  - Auricular cartilage inflammation
  - Nasal chondritis
  - Seronegative polyarthritis
  - Ocular inflammation
  - Audio-vestibular damage

Chest 2009;134(4):1024-1030

# COPD and TBM/EDAC

- 214 patients with chronic bronchitis:
  - 24% with TBM
- 2,150 patients with TBM:
  - 53% concurrent chronic bronchitis
- 8,820 subjects from 21 clinical centers involved in the COPDGene study
  - Paired inspiratory / expiratory CT
  - Measurements at the aortic arch, carina, and bronchus intermedius (BI)
  - EDAC in 443/8,820 subjects (5%)
  - SGRQ worse in EDAC; No difference in 6MWD
  - Patients with EDAC had increased frequency and severity of respiratory exacerbations

J Otorhinolaryngol Relat Spec. 1976;38(3):178-186 // Ann Clin Res. 1977;9(2):52-57 // JAMA 2016;315(5):498-505

# Dynamic expiratory tracheal collapse in morbidly obese COPD patients

- N = 100 (48 F) patients with obesity and COPD
  - N = 53 normal volunteers
  - Expiratory collapse:
    - No significant difference in collapse between healthy volunteers with BMI  $\geq 35$  and  $< 35$
    - Significantly associated with BMI:
      - $69 \pm 12\%$  tracheal collapse among 20 COPD patients with BMI  $\geq 35$
- vs.
- $57 \pm 19\%$  in others (*P-value* = 0.002)

COPD 2013;10(5):604-610

# GERD and TBM/EDAC

- Retrospective analysis
- 45.3% prevalence of GERD (with abnormal esophageal pH test result) in patients with TBM/EDAC
- No reflux symptom correlation in > 50% of patients
- All patients with unsuccessful surgical treatment of TBM/EDAC had severe GERD
- 46% with GERD reported improvement in respiratory symptoms following maximal medical therapy or anti-reflux surgery without requiring further treatment for TBM/EDAC.
  - ✓ Aggressive reflux treatment should be considered in TBM/EDAC patients prior to considering invasive airway procedures or surgery

Chest 2019;155(3):540-545

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- **Clinical manifestations**
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# Clinical manifestations

- Non-specific
  - ✓ Debate on whether TBM/EDAC alone causes symptoms or coexists with other conditions.
- Asymptomatic
- Dyspnea → Respiratory failure
- Cough (*barking seal cough*) → Syncope
- Wheezing
- Mucostasis → Recurrent infections
- Unexplained extubation failure

Ann Clin Res 1977;9:359-364  
Chest 2005;127:984-1005  
Chest 2007;132:609-616  
Chest 2008;134(4):801-807

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# Evaluation

- Functional assessment
- PFT
- Airway oscillometry
- Chest CT (dynamic inspiratory / expiratory)
- Bronchoscopy

# Assessment of symptoms

- Saint George Respiratory Questionnaire (SGRQ)
- Dyspnea index (DI)
- Cough Quality of Life Questionnaire (CQLQ)
- Karnofsky performance status
- ...

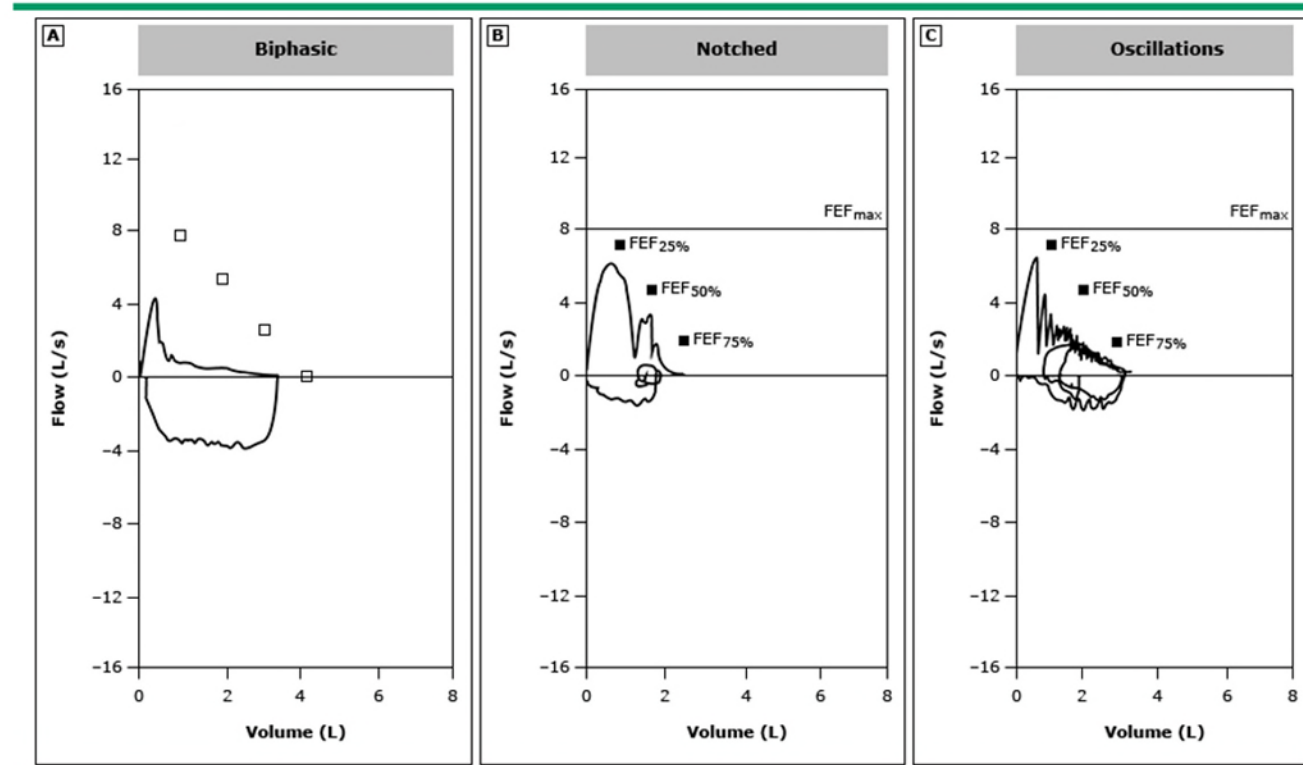
## **MINIMALLY CLINICALLY IMPORTANT DIFFERENCE (MCID)**



# PFT

- Supportive but not diagnostic:
  - 44% obstructive ventilatory defect
  - 18% restrictive defect
  - 17% mixed
  - 21% normal
- Diminished expiratory flow
- Notching / Biphasic / or flow oscillations
- Flow oscillations (“saw-tooth” pattern):
  - TBM
  - OSA
  - Structural or functional disorders of the larynx
  - Neuromuscular diseases

Flow-volume loop characteristics in tracheomalacia



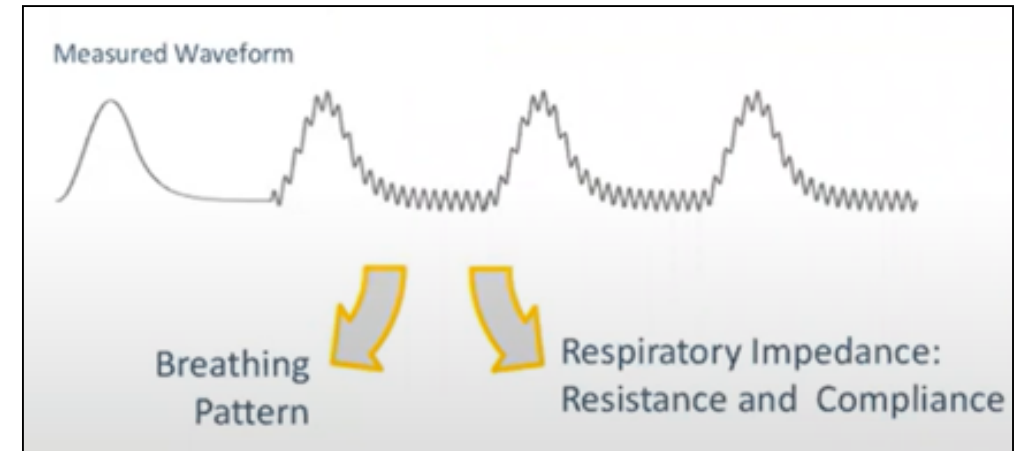
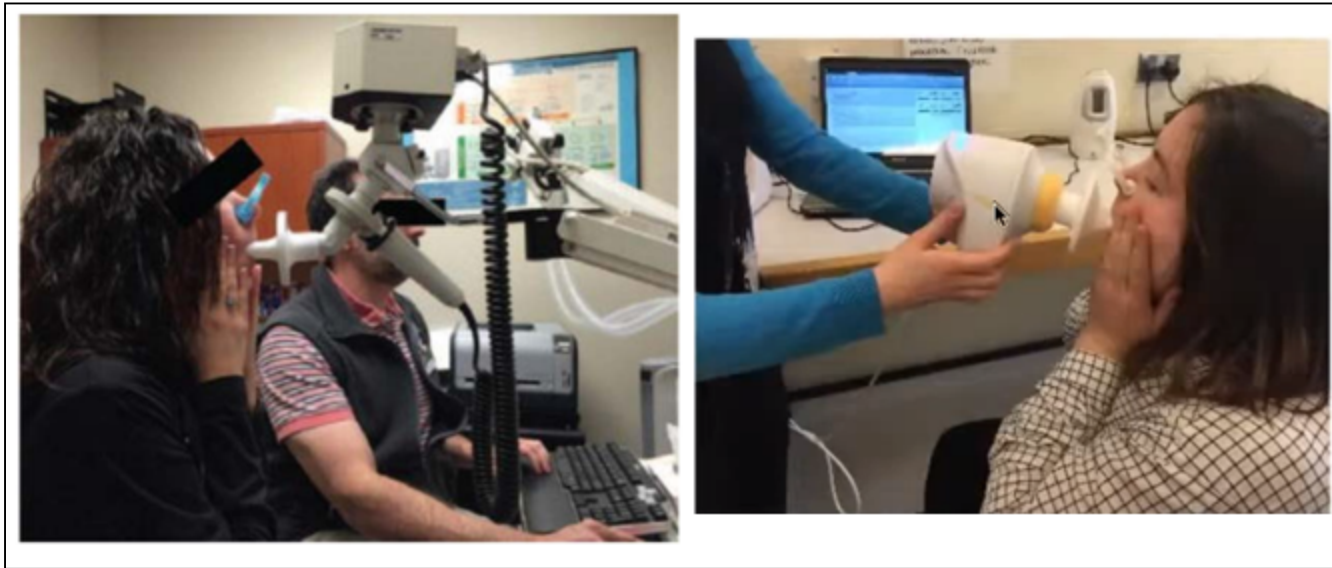
(A) Flow-volume loop in a patient with tracheomalacia demonstrating biphasic morphology with typical obstructive pattern.  
(B) A notched expiratory loop in a different patient is shown.  
(C) Expiratory oscillations from a third patient are shown.

FEF: forced expiratory flow.

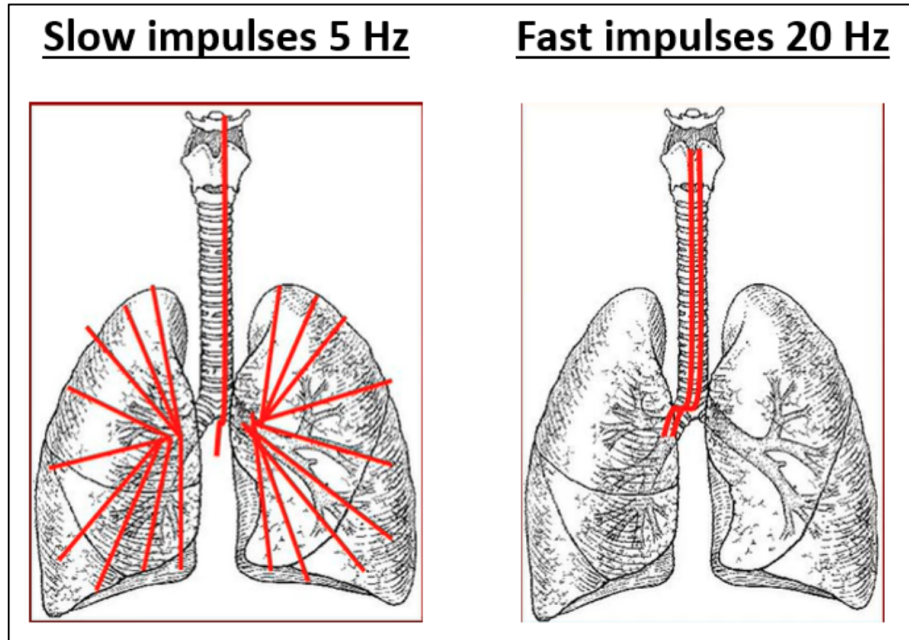
Respiratory Care 2013 VOL 58 NO 9

# Airway oscillometry (AOS)

- Group of techniques for measuring breathing mechanics by superimposing small pressure waves on top of normal tidal breathing.



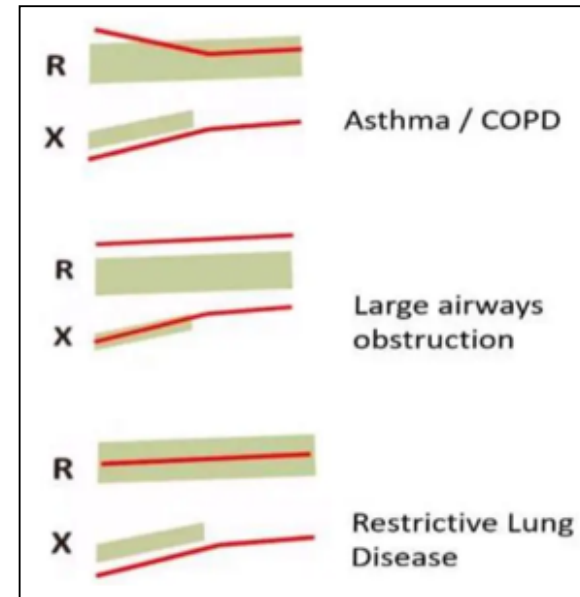
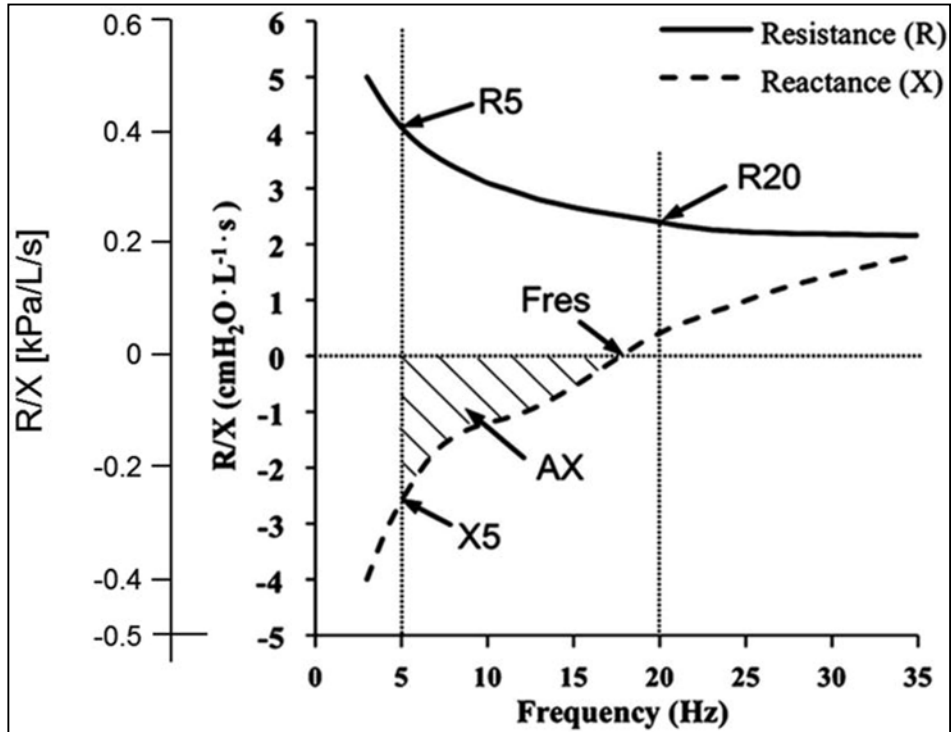
# Airway oscillometry



- Low frequencies:
  - Deep penetration
  - Total airways (central and peripheral)
- High frequencies:
  - Low penetration
  - Upper (large, central) airways

Higher oscillation frequencies are reflected from the larger airways.  
Lower frequencies travel more peripherally before returning to the mouth.

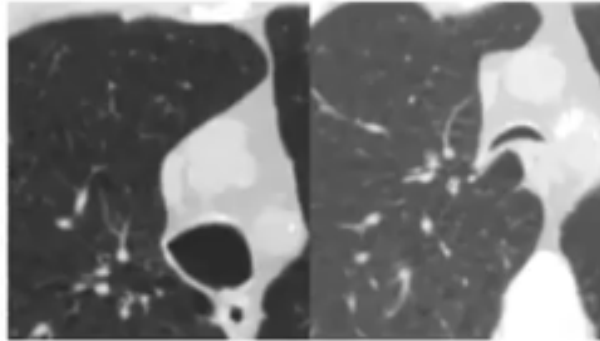
# Airway oscillometry



- Obstruction of the small, distal airways in the peripheral lung causes an increase in resistance (R) with a downward shift in reactance (X). In the presence of heterogeneity, R becomes curved.
- Obstruction of the large, central airways causes a parallel upward shift in resistance (R) while reactance (X) remains largely unchanged.
- Restrictive lung diseases cause a decrease in reactance (X).

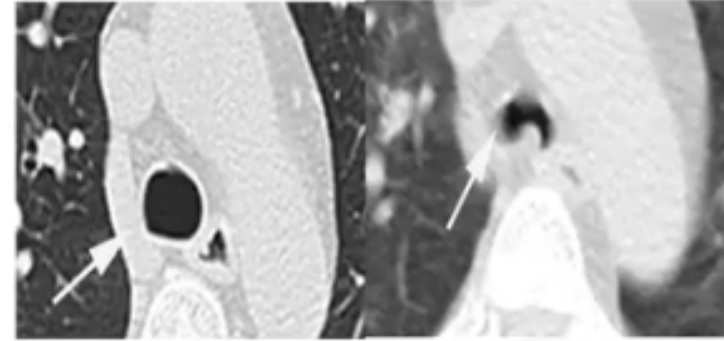
# Dynamic CT chest

## Tracheobronchomalacia (TBM)



Collapse of anterior cartilage

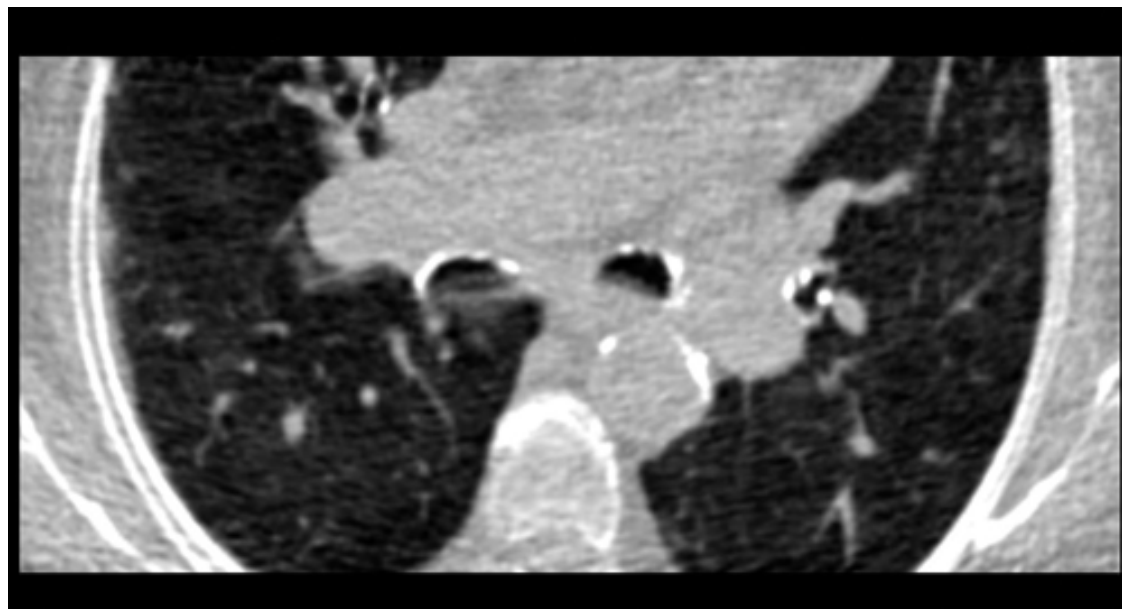
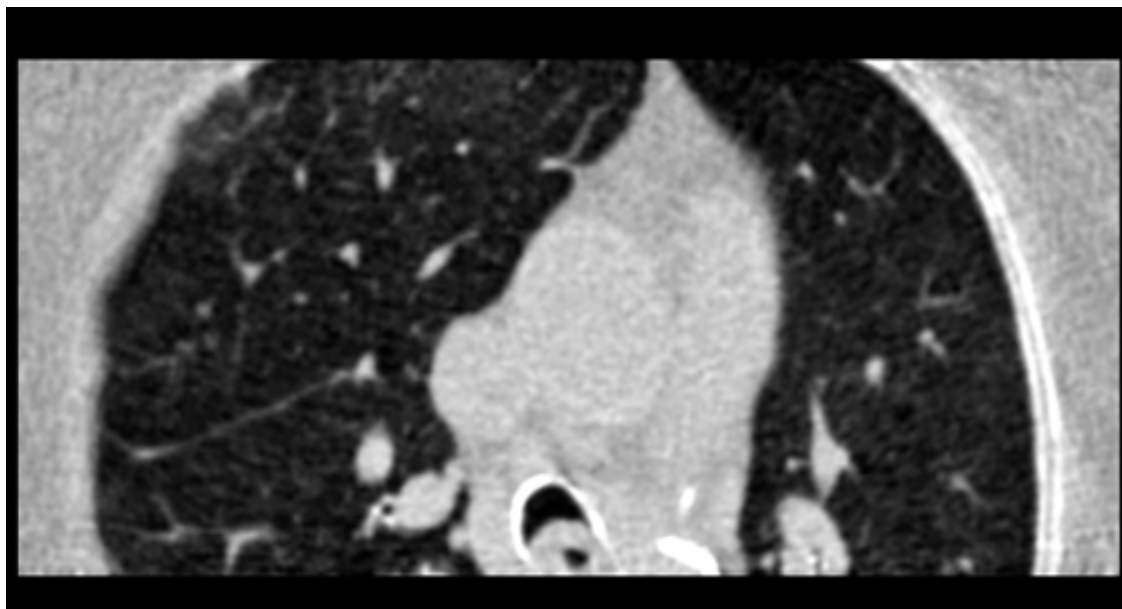
## Excessive Dynamic Airway Collapse (EDAC)



Excessive invagination of posterior membrane

# Dynamic CT chest

Volume acquisition during tidal breathing



Images courtesy of Dr. Mark Hammer, Thoracic Radiology, BWH

# CT – 3D assessment

- Assessment of the trachea requires Multiplanar Reconstruction (MPR) and is often helped with 3D reconstructions



# Bronchoscopy as a diagnostic tool

## 1. “Gold standard” for assessment of airway collapse:

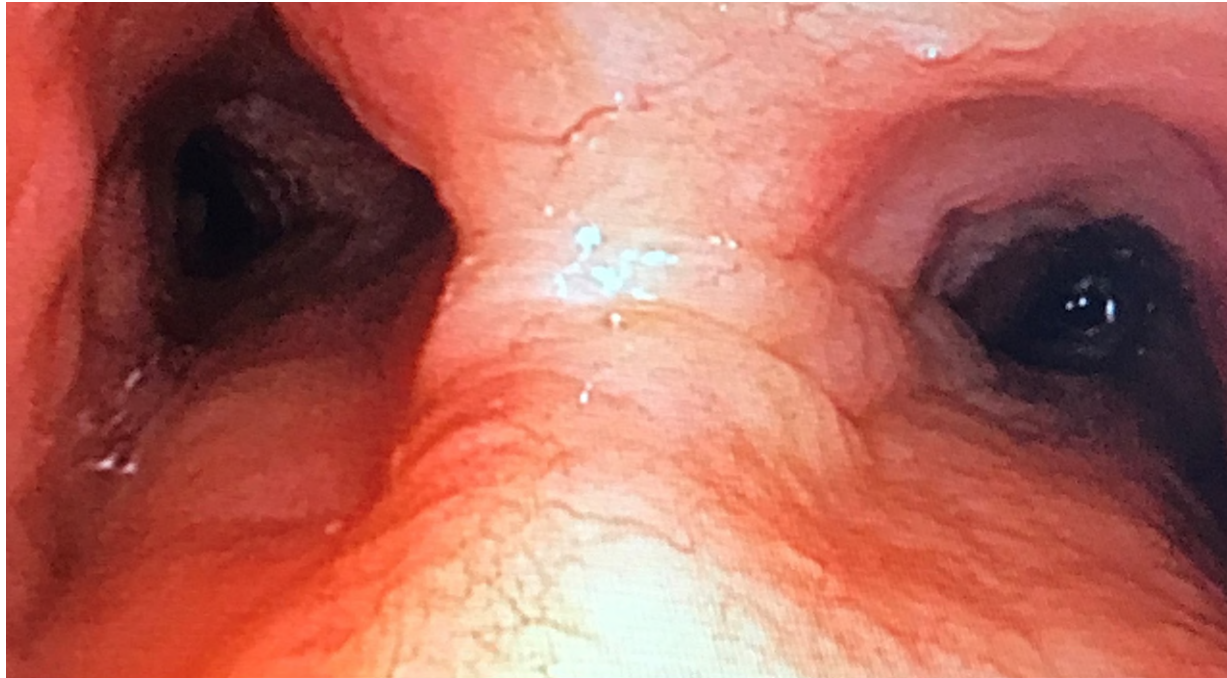
- Approaches to sedation: “awake” ( $\pm$  specific maneuvers) vs. GA (e.g., TIVA)
- What to look for:
  - Degree of collapse (50% reduction? By diameter or cross-sectional area (CSA)?)
  - Extent of airway involvement (central airways only vs. involvement of lobar bronchi and beyond)



# Bronchoscopy as a diagnostic tool

## 2. Better identification of underlying etiology

- Visualization  $\pm$  sampling of airway abnormalities



Tracheobronchial amyloidosis (AL type)

# Bronchoscopy as a diagnostic tool

## 3. Assessment of TBM's (EDAC's) functional impact

- Retained secretions
- “Kissing ulcers”



Menon AA, Shafiq M. Am J Respir Crit Care Med. 2022.

# Bronchoscopy as a diagnostic tool

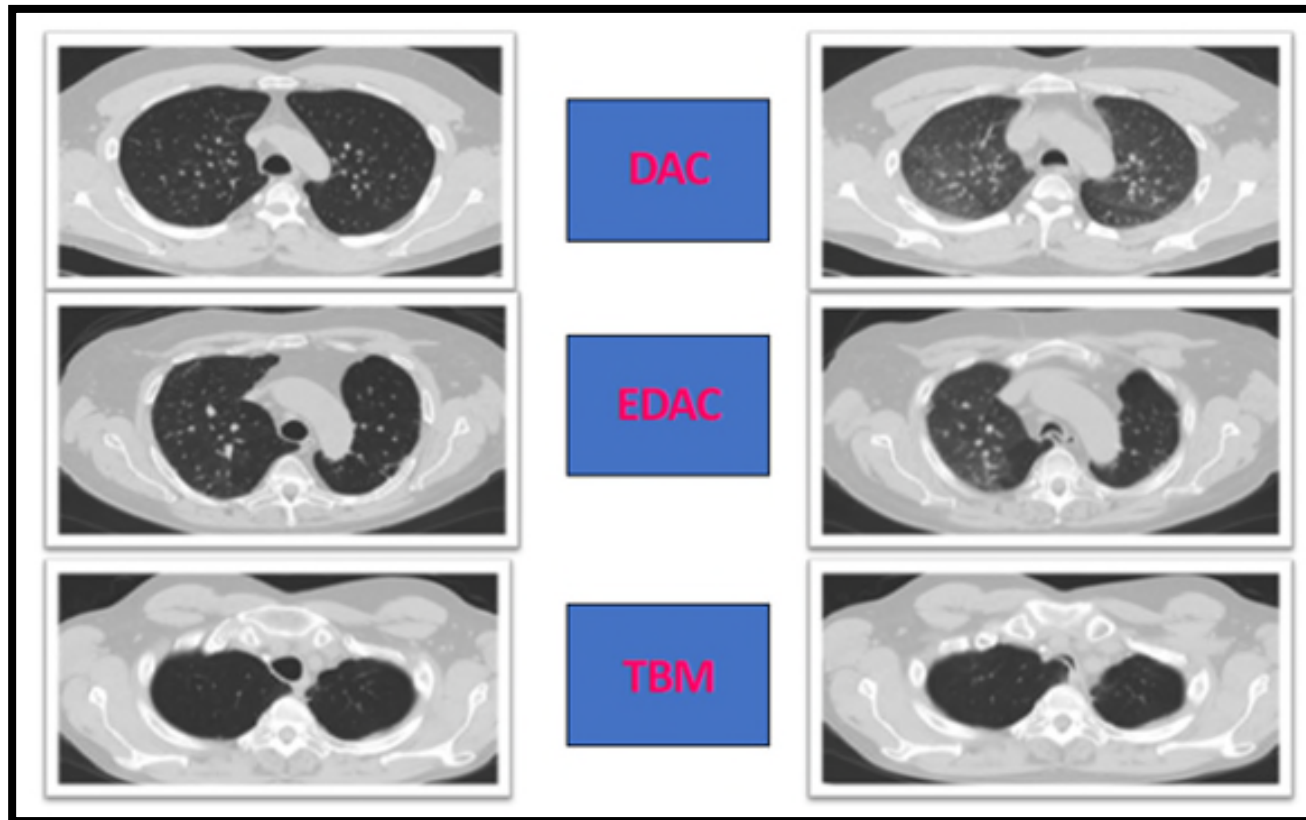
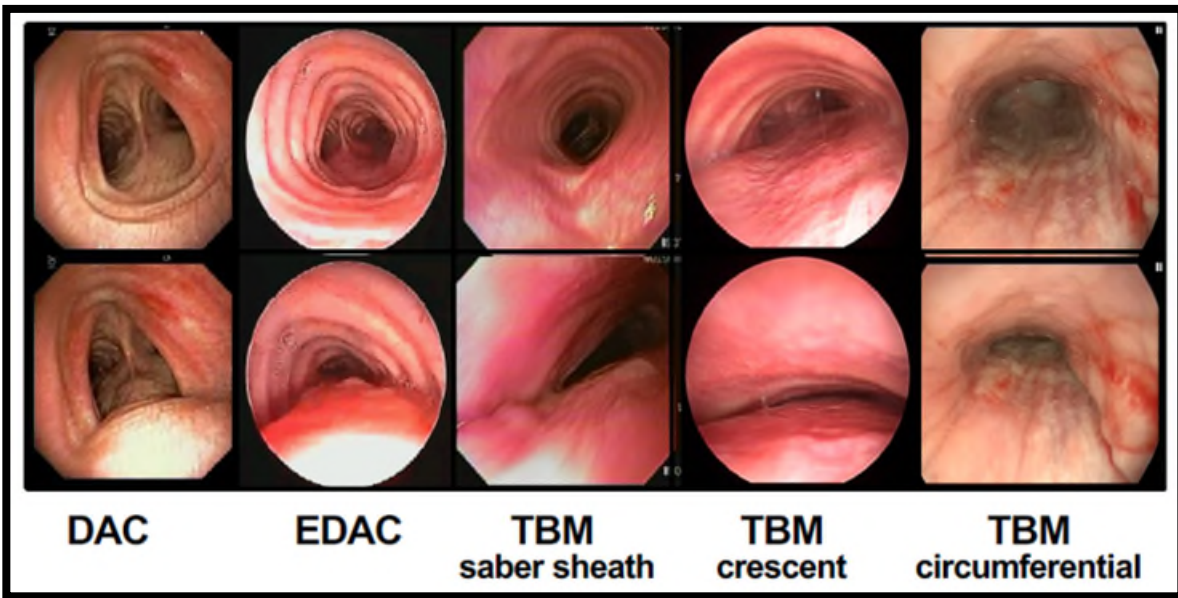
## 4. Assessment of CPAP\* response

- Can attempt titration to lowest possible setting needed to prevent excessive expiratory collapsibility
- Note: APAP (often used for OSA), while helping ensure adequate upper airway patency, may not necessarily use a pressure target that is high enough to overcome tracheobronchial collapsibility

\*CPAP can serve as a “pneumatic splint” and reduce expiratory collapsibility of central airways



Image courtesy of Dr. Ajay Wagh



- | Bronchoscopy  | Computed Tomography                                    |
|---|--|
| 1. Direct visualization of the airway mucosa                  | 1. No details about the mucosa                         |
| 2. Can be performed in critically ill patients at the bedside | 2. Reveals adjacent parenchyma and vascular structures |
| 3. Lack of ionizing radiation                                 | 3. Paired dynamic CT requires patient cooperation      |
| 4. Allows assessment of CPAP response                         | 4. Exposure to ionizing radiation                      |

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# Treatment options



# Medical management

- Avoid ICS if possible?
  - Long-term ICS may contribute to TBM and/or EDAC (smooth muscle atrophy)
- Weight loss (where applicable)
- Optimize management of comorbidities (e.g., COPD, asthma, GERD)
- Airway clearance regimen:
  - Guaifenesin; Hydration; Nebs (e.g., saline)
  - Oscillatory PEP devices (Acapella, Aerobika)
- Positive airway pressure:
  - Pursed lip breathing / Ambulatory PEP device (PEP Buddy)
  - CPAP / Ambulatory CPAP (for night/naps/“TBM/EDAC attacks”)
    - ✓ CPAP acts as a pneumatic stent in TBM
    - ✓ Bronchoscopy can help identify the pressure needed to prevent airway collapse (*titration study*)

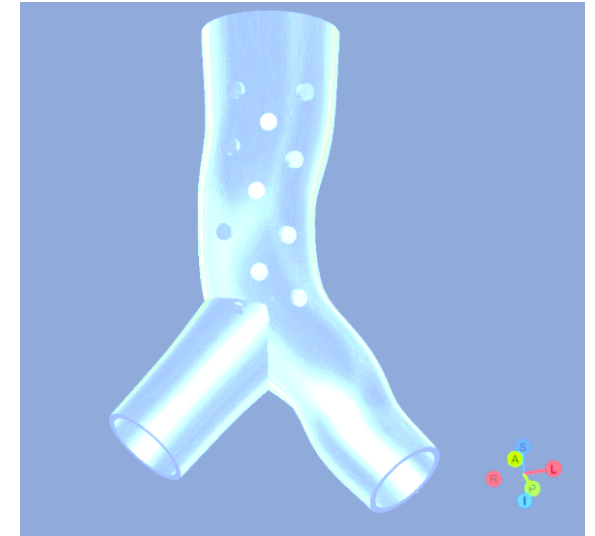


# Role of airway stenting

1. Stent trial as decision aid for surgery
2. Stenting as destination therapy?

# Stent trial as decision aid for surgery

- Stent trial protocol
  - 1-2 weeks, then scheduled removal
  - Objective + (mostly) subjective assessment
    - Some centers reserve stent trials for equivocal cases
- Stent options:
  - Silicone Y-stent
    - Off the shelf vs. 3D printed (customized)
  - SEMS (self-expanding metallic stents)
    - Covered vs. uncovered
    - Note: FDA Black Box warning for use in non-malignant airway disease



Standard vs. customized (3D-printed) silicone Y-stent

# Stent as destination therapy?

- Mucostasis / Respiratory infection
  - Airway clearance can potentially be worse than with TBM itself
  - Mucus plugging can be an airway emergency
- Granulation tissue
  - Hemoptysis
  - Obstruction
- Cough and/or chest pain
- Migration
- Stent fracture
- Epithelialization (uncovered metallic stents only)

# Silicone (Y) as destination therapy?

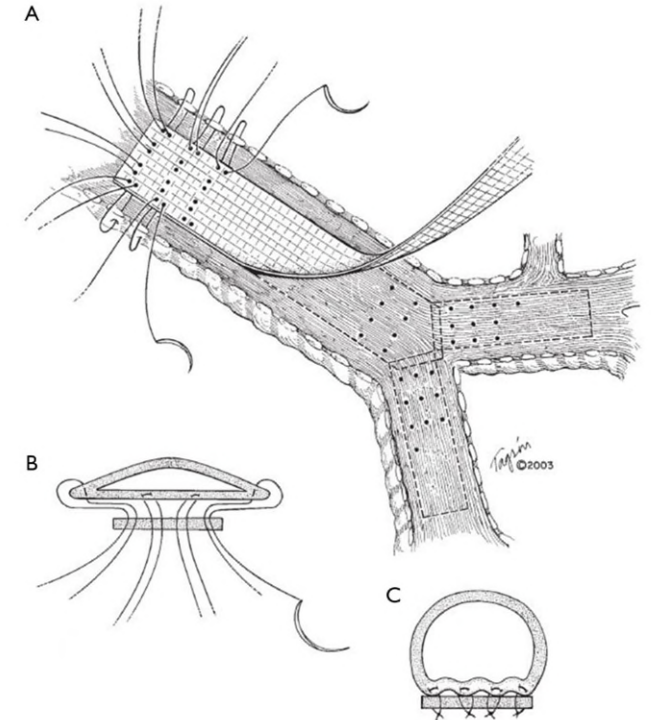
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- Granulation tissue
  - Hemoptysis
  - Obstruction
- Cough and/or chest pain
- ~~Migration~~
- Stent fracture
- ~~Epithelialization (uncovered metallic stents only)~~

# **Stent Tracheostomy** as destination therapy?

- Mucostasis / Respiratory infection
  - ~~Airway clearance can potentially be worse than with TBM itself~~
  - Mucus plugging can be an airway emergency
- Granulation tissue
  - Hemoptysis
  - Obstruction
- ~~Cough and/or chest pain~~
- ~~Migration~~
- ~~Stent fracture~~
- ~~Epithelialization (uncovered metallic stents only)~~

# Gold standard: Surgical tracheobronchoplasty

- What?
  - Prolene mesh connecting one end of each cartilaginous ring to the other (to restore horseshoe shape)
  - Plication of posterior membrane to this mesh (to prevent expiratory collapse)
- How?
  - Open (thoracotomy) – *traditional approach*
  - Minimally invasive:
    - ~~VATS~~
    - Robotic – *newer, less invasive approach*



# Minimally invasive thoracic surgery

- VATS vs. Robotics
- Surgery is in 3-D space-pitch, roll and yaw
  - VATS instruments do not bend
  - Robotic instruments are “wristed”
- Imaging
  - VATS-2-D view (cannot tell depth)
  - Robotic-3-D view (binocular)



# Robotic tracheobronchoplasty: Published data

- **No RCT data available**
- Retrospective study out of New York (single institution) featuring cases b/w 2013-2020
- R-TBP done on 118 patients with suspected TBM (cough, SOB, and/or “chronic pneumonia” who all had severe collapse (>90%) on awake bronchoscopy [no stent trial])

**Improvement in postoperative lung function in patients with moderate to severe airway obstruction after robotic-assisted thoracoscopic tracheobronchoplasty**

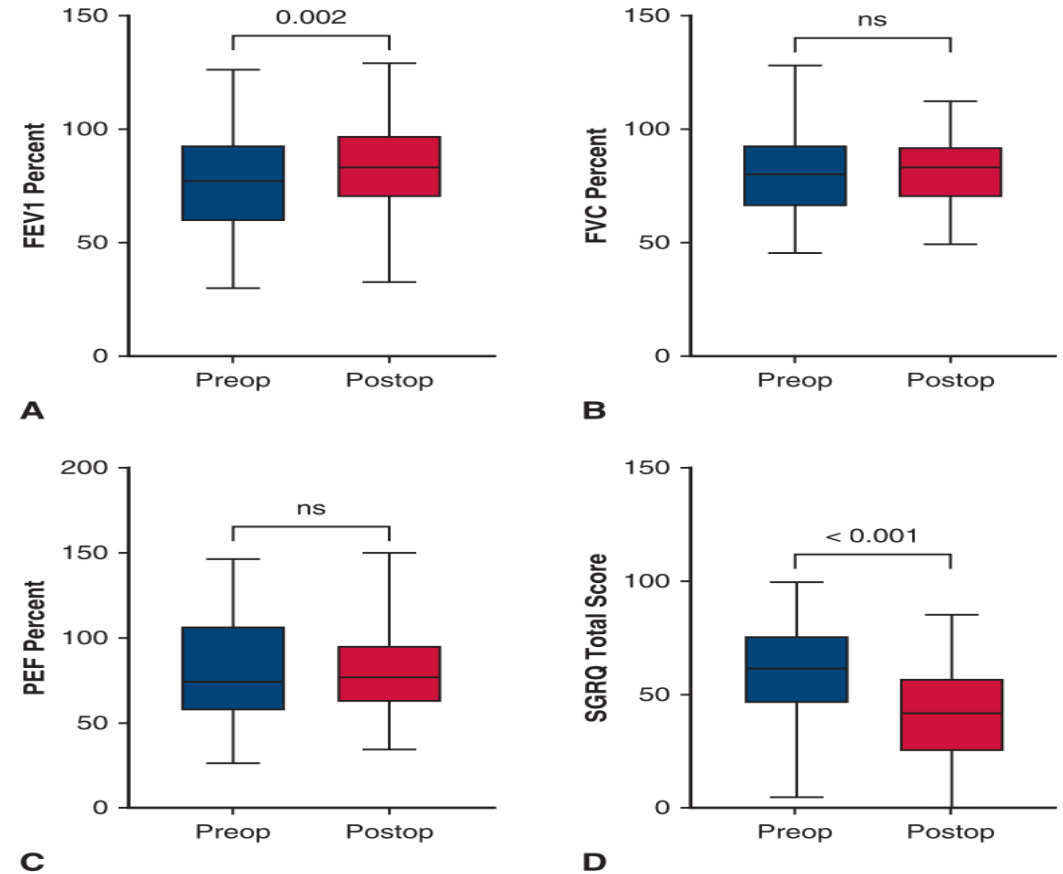
 Check for updates

Matthew L. Inra, MD,<sup>a,b</sup> Gregory A. Wasserman, DO, PhD,<sup>a,b,c</sup> Jason Karp, MD,<sup>b,d</sup> Stuart Cohen, MD,<sup>b,e</sup> S. Jacob Scheinerman, MD, FACS,<sup>a,b</sup> and Richard S. Lazzaro, MD, FACS<sup>a,b,f</sup>

*Journal of Thoracic and Cardiovascular Surgery. 2023*

# Robotic tracheobronchoplasty: Follow up

- At median of 16 months [IQR 5-29]:
  - Significant improvement in FEV1 (77%  $\rightarrow$  83%;  $p = 0.002$ )
- At median of 7 months [IQR 3-16 months]:
  - Improved SGRQ scores (61  $\rightarrow$  42;  $p < 0.001$ )



*Journal of Thoracic and Cardiovascular Surgery. 2023*

# Robotic tracheobronchoplasty: Costs and risks (detailed in an earlier study by the same group)

- Median hospital LOS: 3 days
- Complications: 19 (45%)
  - Minor: 11 (26%)
  - Major: 8 (19%)
    - 2 pneumothorax episodes needing chest tube
    - 2 SC emphysema episodes needing infraclavicular blowholes
    - VATS evacuation for hemothorax post-chest tube on POD2
    - Revision surgery for persistent symptoms (POD 125)
    - 1 return to ICU (needing bronchoscopy)
    - 1 return to ICU for arrhythmia (tachy-brady syndrome)
    - 0 deaths | 0 reintubations or tracheostomies

# Multi-disciplinary approach to TBM/EDAC

## *Our BWH TBM/EDAC program*

- Integrated collaboration: Pulmonary, Interventional Pulmonology, Thoracic Surgery, Radiology, ENT, and Anesthesiology
- Interdisciplinary evaluation of complex airway cases
- Advanced diagnostic tools: cine CT, airway oscillometry, 3D-printed stenting
- Innovative therapies: robotic-assisted thoracoscopic tracheobronchoplasty
- Platform for research and development of novel TBM/EDAC interventions

## Pulmonary Medicine:

- Adel El Boueiz
- Gary Visner (BCH)
- Chris Fanta

## Interventional Pulmonary:

- Majid Shafiq
- Hisashi Tsukada
- Anuradha Ramaswamy

## Anesthesiology:

- Stephanie Yacoubian



## Thoracic Surgery:

- Matt Rochefort
- Antonio Coppolino
- John Wain
- Ben Zendejas-Mummert
- Matt Pommerening
- Hassan Khalil

## Radiology:

- Mark Hammer
- Noby Hata

## ENT:

- Christopher Dwyer
- Thomas Carroll

# Conclusions

- TBM / EDAC:
  - Often under-recognized and frequently misdiagnosed
  - Heterogeneous disorder with diverse symptom profile
  - Untreated disease associated with substantial morbidity and healthcare utilization
  - Lack of standardized definition and classification
  - Advances in CT, bronchoscopy, and multidisciplinary care improving diagnosis and management
- Tracheobronchoplasty → symptomatic improvement in selected TBM patients
  - Modern open and robotic techniques enhance procedural safety
- Continued research will refine understanding and guide future care



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**THANK  
YOU**

