Tracheobronchomalacia and Excessive Dynamic Airway Collapse

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DEFINITIONS AND CLASSIFICATIONS
Unambiguous definitions and clinically useful classifications provide a common language for health care providers managing expiratory central airway collapse (ECAC). By applying accepted terminology in their practices, clinicians and scientists can stratify patients according to predefined objective criteria and analyze data. Consensual frameworks offered by classification systems allow comparison of data within populations over time and between populations at the same point in time, thus facilitating meaningful research.1,2

KEY POINTS
• Tracheobronchomalacia is characterized as weakened or destroyed cartilage in the central airways resulting in expiratory flow limitation.
• Excessive dynamic airway collapse is characterized by excessive bulging of the posterior membrane inside the central airway lumen.
• A careful physiologic assessment of the impact of expiratory central airway collapse on airflow and functional status is warranted before treatment.
• Identification of the flow-limiting airway segments can be obtained by performing functional bronchoscopy before invasive interventions.
• Even when the central airway collapse is identified as responsible for symptoms, we suggest a conservative approach with medical treatment and noninvasive positive pressure ventilation before committing patients to potentially harmful effects resulting from airway stents or open surgical procedures.

In this regard, the collapse of the intrathoracic trachea and mainstem bronchi in adult patients has been described using a variety of terms, including tracheobronchomalacia (TBM), tracheobronchial collapse, expiratory tracheobronchial collapse, expiratory tracheobronchial stenosis, tracheobronchial dyskinesia, dynamic airway collapse (AC), and ECAC.3 However, these terms do not distinguish between collapse of the pars membranosa and collapse of the cartilaginous wall. ECAC is an accepted term to describe the narrowing of the central airways during expiration; it is a

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syndrome comprising 2 different pathophysiologic entities: TBM, characterized by weakness of the tracheobronchial cartilaginous structures, and excessive dynamic AC (EDAC), defined as excessive bulging of the posterior membrane into the airway lumen during expiration without cartilage collapse.\(^6\)\(^{-}\)\(^{10}\)

A major controversy in the published literature and among experts managing these patients is represented by the amount of collapse labeled as excessive. The frontier between normal and abnormal narrowing of the central airways during exhalation has not been clarified, and investigators propose various cutoff values.\(^6\)\(^{-}\)\(^{12}\) There is variability among studies in regards to anatomic location and respiratory maneuver used to measure narrowing of the expiratory airway (Table 1).\(^10\)\(^{-}\)\(^{15}\) These facts may be the main source of inconsistency in reported prevalence of these disorders. The anatomic site used for measuring the collapse needs to be standardized, because physiologic airway narrowing is more pronounced in the bronchus intermedius and main carina than at the aortic arch or cricoid level.\(^12\)

Results of dynamic computed tomography (CT) studies show that 70% to 80% of normal individuals meet the 50% criteria used for abnormal collapse.\(^6\)\(^{,}\)\(^{12}\)\(^{,}\)\(^{16}\) Healthy volunteers with normal lung function have shown mean levels of expiratory collapse of 54% in the trachea, 67% in the right main bronchus (RMB), 61% in the left main bronchus (LMB), and even total collapse in the bronchus intermedius.\(^12\) A different study showed that the mean % collapse of normal volunteers was 66.9% in the RMB and 61.4% in the LMB, with 73% of participants exceeding the currently accepted cutoff value of 50% threshold for defining bronchomalacia.\(^17\) Even in a disease process such as chronic obstructive pulmonary disease (COPD), in which the central AC is more pronounced, the degree of narrowing may be independent of disease severity and does not correlate significantly with physiologic parameters.\(^5\)\(^{,}\)\(^{11}\) Excessive expiratory tracheal collapse defined as more than 80% expiratory reduction in tracheal luminal cross-sectional area during dynamic CT was shown to not significantly correlate with the pulmonary function tests (PFTs) or quality-of-life (QOL) measures.\(^6\)\(^{,}\)\(^{11}\)

To reduce false-positive diagnoses and avoid unwarranted treatments, EDAC may be defined only if clinically relevant excessive collapse is noted during tidal breathing (Fig. 1). The degree of pathologic expiratory collapse has not yet been established on physiologic basis because work of breathing and symptoms depend not only on the degree of airway narrowing but also on its geometry and flow velocity.\(^18\) Therefore, the accurate assessment of the reduction in airway lumen cross-sectional area becomes relevant for the purpose of having a common language when evaluating patients and communicating about TBM and EDAC, and not necessarily only to decide on need for therapeutic interventions.

The degree of narrowing is only 1 factor involved in flow limitation; it is only 1 criterion included in classifications for this syndrome. Most systems are limited by inconsistent definitions or by criteria addressing only the extent, severity, or cause but not the 2 separate morphologic types of TBM and EDAC or the patient’s functional impairment (Table 2).\(^10\)\(^{-}\)\(^{15}\)\(^{,}\)\(^{19}\) A classification based on objective quantifiable criteria has been developed and can be applied before and after therapeutic interventions to objectively document not only the changes in the extent and severity of AC but also the impact of these changes on functional class (Table 3).\(^2\) The criteria of this system can be grouped in 2 sets: the descriptive factors including morphology and etiology, and stratification factors that can be scored objectively. The morphology criterion describes the shape of the airway lumen, which is reduced during expiration as assessed by bronchoscopy or radiologic studies. ECAC has 5 morphologic types (Fig. 2). Origin (etiology) describes the underlying mechanism responsible for the abnormality: idiopathic or secondary to other disorders (Table 4). To describe functional class, this system used the World Health Organization functional impairment scale, because of its easy clinical applicability and because it does not address just dyspnea but the overall impact of symptoms on patient’s functional status. The extent criterion describes the location and distribution of the abnormal airway segment as assessed by bronchoscopy or radiographic studies. The severity criterion describes the degree of the AC during expiration as assessed by bronchoscopy or radiographic studies. Since its introduction in 2005, the terminology proposed in this system has been applied in clinical research of these disorders.\(^5\)\(^{,}\)\(^{6}\)\(^{,}\)\(^{20}\)\(^{-}\)\(^{24}\) This classification allows monitoring of the progression or improvement of the disease process and the outcome and durability of different treatment strategies on airway lumen patency and patient symptoms. Five domains are addressed: functional class (F), extent (E), morphology (M), origin (O), and severity of AC (S). The F, E, and S parts of the system have an ordinal scale of 1 to 4 (see Table 3). Outcomes are documented as subscripts, for example $F_2\ E_2\ S_4$, and should not be combined to form a single number. This information can be tabulated or plotted to provide a visual temporal treatment...
<table>
<thead>
<tr>
<th>Reference</th>
<th>Cutoff Value to Define Abnormal, Excessive AC During Expiration</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Aquino et al, 7 2001</td>
<td>&gt;28% expiratory reduction in sagittal diameter&lt;br&gt;18% expiratory reduction in CSA in the upper trachea&lt;br&gt;28% expiratory reduction in CSA in the middle trachea</td>
<td>Only for tracheal collapse&lt;br&gt;Used paired inspiratory–static end-expiratory CT</td>
</tr>
<tr>
<td>Stern et al, 8 1993</td>
<td>35% expiratory reduction in CSA in normal individuals</td>
<td>Only for tracheal collapse&lt;br&gt;Used paired inspiratory–dynamic–expiratory CT</td>
</tr>
<tr>
<td>Nuutinen, 9 1977</td>
<td>&gt;50% expiratory reduction in sagittal diameter</td>
<td>For tracheal and bronchial collapse&lt;br&gt;Used bronchoscopic estimations</td>
</tr>
<tr>
<td>Zhang et al, 75 2003</td>
<td>&gt;50% expiratory reduction in CSA</td>
<td>Only for tracheal collapse&lt;br&gt;Low-dose CT (40–80 mA) was just as accurate as the standard dose (240–280 mA)&lt;br&gt;Used paired inspiratory–dynamic–expiratory CT</td>
</tr>
<tr>
<td>Gilkeson et al, 130 2001</td>
<td>&gt;50% expiratory reduction in CSA</td>
<td>For tracheal and bronchial collapse&lt;br&gt;Paired inspiratory–dynamic–expiratory CT</td>
</tr>
<tr>
<td>Hein et al, 66 2000</td>
<td>&gt;50% expiratory reduction in CSA</td>
<td>Only for tracheal collapse&lt;br&gt;Used paired inspiratory–dynamic–expiratory electron beam tomography</td>
</tr>
<tr>
<td>Boiselle et al, 12 2009</td>
<td>&gt;50% expiratory reduction in CSA</td>
<td>Only for tracheal collapse in healthy volunteers&lt;br&gt;Used low-dose paired inspiratory–dynamic–expiratory CT&lt;br&gt;80% of healthy study participants met the criteria for abnormal collapse</td>
</tr>
<tr>
<td>Litmanovich et al, 17 2010</td>
<td>&gt;50% expiratory reduction in CSA</td>
<td>Only for bronchial collapse&lt;br&gt;Used low-dose paired inspiratory–dynamic–expiratory CT&lt;br&gt;73% of healthy participants exceeded the diagnostic threshold level for abnormal bronchial collapse</td>
</tr>
<tr>
<td>Masaoka et al, 10 1996</td>
<td>&gt;80% expiratory narrowing</td>
<td>For tracheal and bronchial collapse&lt;br&gt;Used bronchoscopic estimations and frontal and lateral radiograph films to estimate the narrowing&lt;br&gt;Narrowing is not clearly defined as reduction of CSA or reduction in diameter</td>
</tr>
<tr>
<td>Boiselle et al, 6 2012</td>
<td>&gt;80% expiratory reduction in CSA</td>
<td>Only for tracheal collapse in patients with COPD&lt;br&gt;Used low-dose paired inspiratory–dynamic–expiratory CT</td>
</tr>
</tbody>
</table>

*Abbreviations: COPD, chronic obstructive pulmonary disease; CSA, cross-sectional area; CT, computed tomography.*
map, charting patient progress through treatment. In this article, a description is given of how this system can be used in 2 clinical scenarios: TBM and EDAC.

**Clinical Application: TBM**

A patient with a history of extensive mediastinal lymph node calcifications and bilateral upper lobe fibrosis was unable to clear secretions, had progressive dyspnea on exertion, and cough limiting normal physical activities. The patient was treated for asthma with inhaled and systemic steroids for more than a year before a bronchoscopy, which revealed collapse of the anterior wall of the lower trachea. During tidal expiration, this collapse reached a 100% closure of the lumen (Fig. 3). This morphology was characteristic of crescent-type malacia and was considered to be caused by secondary tracheobronchomegaly (caused by bilateral upper lobe fibrosis). Because of the patient’s lack of discomfort at rest, but presence of increased symptoms with normal physical activity, his functional class was labeled as F2. The process was limited to the lower trachea, therefore the extent was labeled E2, and because the 2 walls of the trachea were touching each other during expiration (100% closure), severity of airway narrowing was labeled as S4. Rigid bronchoscopy was performed and a straight silicone stent inserted in to the lower trachea. After intervention, the patient was tapered off the steroids for his presumed asthma and symptoms improved to normal (F1). Bronchoscopy showed no residual malacia (E1) and normal expiratory airway lumen (S1) (see Fig. 3).
Clinical Application: EDAC

A patient with COPD and obesity presented with worsening dyspnea. She had a history of severe oxygen and corticosteroid-dependent COPD limiting her daily activities. The main finding on bronchoscopy was bulging of the posterior membrane in the lower trachea during tidal breathing, with narrowing of the airway lumen by 100% at the level of main carina. This finding was consistent with EDAC morphology. The findings extended in the lower tracheal and mainstem bronchi, and the extent was labeled E4; the severity was S4 (100% closure during exhalation), and given her symptoms with minimal activity, functional class was F3. The patient underwent a Y silicone stent insertion, and after this procedure, she was classified as F2 E1 S1 (see Fig. 3). The lack of complete symptomatic response to stent insertion was explained by confounding disorders (COPD and obesity) and by the choke point migration seen just distal to the stent (see Fig. 3).

Flow-Limitation Theories

Equal pressure point theory: dynamic compression and determinants of maximal expiratory flow

There is a region within the intrathoracic airway where intraluminal and extraluminal pressures become equal once expiratory flow becomes limited at a given lung volume. The point within the airway at which this situation occurs is called the equal pressure point (EPP) (Fig. 4). This concept is based on the following facts: alveolar pressure is the driving pressure that causes gas to flow through airways during expiration. This pressure (Palv) is determined by the recoil pressure of the lungs (Pst) and the pleural pressure (Ppl):

\[
\text{Palv} = \text{Ppl} + \text{Pst}
\]  
(1)

A pressure decrease is required to accelerate air as it moves from an upstream (toward the alveoli) region of low velocity to a downstream (toward the mouth) region of high velocity. Because of this pressure decrease, the intraluminal pressure (P L) eventually becomes equal to pleural pressure (Ppl). The point in the airway at which this process occurs, the EPP, divides the airways into upstream segments (alveolarward from the EPP), at which transmural pressure (P L–Ppl) is positive, and downstream segments (mouthward from the EPP), at which the transmural pressure is positive within the extrathoracic airways and negative within the intrathoracic airways. For a given lung volume, driving pressure upstream from the EPP would be equal to lung elastic recoil (driving pressure = Palv–P L, but at EPP, P L = Ppl and based on Equation 1, driving pressure = Pst and becomes effort independent); downstream from the EPP, airways are compressed during expiration (see Fig. 4). This region of airway compression is referred to as a flow-limiting segment (FLS). This compressed airway segment develops close to the EPP where Ppl exceeds P L and where there is absence or inadequate cartilaginous support or traction provided by neighboring alveoli. This situation explains collapse of the trachea and mainstem bronchi at the weakest point in the airway wall, namely the pars membranosa, which is not supported by airway cartilage.

As lung volume decreases during expiration, elastic and alveolar pressures are reduced with respect to pleural pressure, and EPP moves toward the alveoli. This situation results in a lengthening of the increasingly narrow downstream segment. This lengthening can be seen on bronchoscopy or dynamic CT as EDAC (see Fig. 4). Thus, the FLS have tracheal location at high lung

PATHOPHYSIOLOGY

TBM and EDAC have different morphology on imaging studies and bronchoscopy. The 2 processes are also distinct in terms of impact on flow dynamics. Physiologic studies addressing the collapse of the central airways suggest that EDAC is likely a consequence of peripheral airway obstruction from emphysema, chronic bronchitis, or asthma or resulting from the restrictive physiology and positive pleural pressures in morbid obesity. TBM, on the other hand, is a true central airway cartilaginous disease resulting in AC and flow limitation. Theories and mathematical models have been proposed and tested to explain expiratory flow limitation in health and obstructive ventilatory disorders and are relevant to understanding flow limitation in EDAC and TBM.
Table 2
Classification systems used for ECAC

<table>
<thead>
<tr>
<th>Reference</th>
<th>Criteria Included in the System</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Rayl,13 1965</td>
<td>Extent: proximal (type I), mediastinal (type II), and intrapulmonary (type III) airways</td>
<td>Tracheobronchial collapse was assessed during cough on cinebronchography</td>
</tr>
<tr>
<td>Johnson et al,14 1973</td>
<td>Severity: 4° of airway narrowing</td>
<td>TM: &gt;50% collapse during coughing on fluoroscopy</td>
</tr>
<tr>
<td>Feist et al,15 1975</td>
<td>Cause: congenital and acquired</td>
<td>TM: &gt;50% collapse during coughing on fluoroscopy</td>
</tr>
<tr>
<td>Jokinen et al,19 1977</td>
<td>Severity: mild (&lt;50%), moderate (50%–75%), severe (100%)</td>
<td>TBM: expiratory reduction of 50% or more in the anteroposterior diameter of the airways First classification based on bronchoscopic findings</td>
</tr>
<tr>
<td>Mair et al,131 1992</td>
<td>Cause: congenital (type 1), extrinsic compression (type 2), acquired (type 3) Severity: mild (&lt;70%), moderate (70%–90%), severe (&gt;90%) collapse</td>
<td>Described for pediatric TBM Empirical severity score</td>
</tr>
<tr>
<td>Masaoka et al,10 1996</td>
<td>Cause and extent criteria Pediatric, adult, and secondary</td>
<td>TBM: &gt;80% collapse during expiration Based on bronchoscopic estimations and frontal and lateral radiograph films to estimate the narrowing</td>
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</table>

Abbreviations: BM, bronchomalacia; TM, tracheomalacia.

Table 3
Stratification factors from FEMOS classification system for ECAC

<table>
<thead>
<tr>
<th>Definition</th>
<th>Criterion Grade</th>
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<td></td>
<td>1</td>
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<tr>
<td>Functional status</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Extent</td>
<td>No abnormal AC</td>
</tr>
<tr>
<td>Severity</td>
<td>Expiratory AC of 0%–50%</td>
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volumes (i.e., total lung capacity [TLC]), but as lung volume decreases during exhalation, FLS move peripherally but still stay in the central airways (in the lobar, segmental, and at the most subsegmental bronchi), as shown in previous experimental and human studies. Even at residual volume (RV), the FLS were found in the central airways, fixed and in parallel in the right middle lobe, left upper lobe, and left lower lobe bronchi. These lobar and segmental locations of FLS were shown in normal individuals and individuals with obstructive ventilatory impairment over considerable ranges of lung volume. Based on the EPP theory, if the FLS are located in the lobar or segmental airways, then the downstream resistance should not affect flow. Intraluminal pressure monitoring with airway catheters shows the lack of decrease in pressure in airways between the mouth and the FLS. Therefore, tracheal and mainstem bronchial collapsibility observed on dynamic bronchoscopy or dynamic CT in the form of EDAC should not impede flow.

The EPP theory explains how lung compliance and airway resistance affect airflow limitation and how changes in these 2 factors result in increased compression of the airway downstream from the FLS responsible for the bronchoscopic or radiographic EDAC. For instance, a decrease in elastic recoil of the lungs (either because of low lung volume as seen in morbid obesity or because of emphysema) reduces the airway pressure relative to pleural pressure, resulting in greater dynamic compression. A decrease in elastic recoil of the lungs results in less traction on the adjacent airways and therefore greater dynamic compression. As for airway resistance, the greater the pressure decrease along the airway from the alveoli to the EPP (along the upstream segment), the sooner the development of an EPP and the greater the dynamic compression. The EPP theory, therefore, sustains the theory that central airway compression downstream from EPP (bronchoscopic/radiographic EDAC) is not pathologic from a flow dynamic standpoint.

Fig. 2. Morphologic types of ECAC based on the shape of the airway lumen during expiration. (A) Normal dynamic airway compression during exhalation with the posterior membrane slightly bulging within the airway lumen (arrow). This compression usually narrows the airway lumen by less than 50%. (B) In EDAC, the posterior membrane bulges in (arrow) and excessively narrows the airway lumen by 50% or more. This process occurs without cartilaginous wall weakness. (C) In crescent-type TBM, the anterior cartilaginous wall is weakened and collapses inside the lumen (large arrow). (D) In sabre-sheath TBM, the lateral walls are collapsing inside the lumen (arrows). (E) In circumferential-type TBM, typically seen in relapsing polychondritis, the anterior and lateral cartilaginous walls are collapsing inside the lumen (large arrows) and there is diffuse airway edema and hyperemia. The small arrows denote normal expected physiologic dynamic compression, whereas the large arrows denote abnormal airway wall collapse.
Wave speed theory: airway compliance and impact on choke point physiology

A different approach to explain expiratory flow limitation is offered by the wave speed theory, which states that flow limitation in elastic tubes occurs at the speed at which the fluid (e.g., air) in the tube (e.g., airways) propagates pressure waves. These waves develop from the interaction of recoil force of the elastic airway wall and the axial inertial force of the flowing gas. The wave speed is the speed at which a small disturbance travels in a fluid-filled compliant tube. Thus, expiratory flow limitation occurs when flow velocity equals the speed of propagation of pressure pulse waves at some point within the tubes; this point, called the choke point or FLS, tends to be at a region of minimum CSA and minimum intraluminal airway pressure when maximal flow has been reached:

\[ V_{ws} = \frac{A}{\sqrt{\rho C_{aw}}} \]

This wave-speed flow \( V_{ws} \) depends on the CSA \( A \), airway compliance \( C_{aw} \), and density of air \( \rho \).
Fig. 3. TBM case (upper panel): (A) Bronchoscopic image during tidal respiration: lower tracheal lumen during inspiration; (B) lower tracheal lumen during expiration showing 100% closure resulting in severity grade S4; (C) paired inspiratory–dynamic-expiratory CT showing lower tracheal lumen during inspiration; (D) lower tracheal lumen during expiration shows that in addition to the normal dynamic airway compression (small arrow), there is flattening of the anterior wall of the lower trachea (large arrow), consistent with focal (E2) crescent-type tracheomalacia; (E) rigid bronchoscopic image after stent insertion during inspiration; (F) bronchoscopic image during tidal expiration shows patent airway with no residual malacia (E1) and normal airway caliber (S1). EDAC case (lower panel): (G) lower tracheal lumen during inspiration; (H) during tidal expiration, the collapse of the posterior membrane closes the airway completely, resulting in severity grading (S4); (I) paired inspiratory–dynamic-expiratory CT shows normal cartilaginous wall configuration; (J) during expiration, the excessive collapse of the posterior membrane is noted (large arrow), consistent with EDAC. The findings extended to mainstem bronchi, resulting in extent grading of E4. (K) After stent insertion, there was maintained airway patency with no AC (S1). (L) Follow-up bronchoscopy shows AC distal to the left and right bronchial arms of the Y silicone stent, consistent with migration of choke points.
which is the slope of the curve describing \( A \) as a function of transmural pressure \( (P_{tm} = P_L - P_{pl}) \), and the density \( (\rho) \) of the gas, according to Equation 2. A functional definition for choke points is as follows: the most downstream (mouthward) points where the airway pressure does not change with driving pressure. Intraluminal airway catheters can be used to localize choke points by measuring airway pressure during induced flow limitation by decreasing the downstream pressure. This concept has led to the development of intraoperative location of the choke point techniques that might predict response to stent insertion.37

From Equation 2, it can be seen that \( \dot{V} \) ws decreases when \( A \) becomes smaller, and \( Caw \) and \( \rho \) become larger, as would be the case for a hyper-compliant intrathoracic airway during expiration as seen in TBM. Increasing central airway compliance increases airway resistance and decreases maximum expiratory flow, which contributes to the airflow limitation in TBM, characterized by hyper-compliant airways. Results from studies of airflow limitation in theoretic, experimental models and clinical studies show that when the collapsing trachea is supported by a rigid tube, airflow improves and the choke point could migrate from the central airway toward the periphery.38-40 In addition, \( \dot{V} \) ws
indirectly depends on the lung elastic recoil pressure (Pst) and the pressure loss (Pfr) upstream from the choke point, because a decreased pressure head (defined as Pst–Pfr) makes the distending transmural pressure (Ptm) smaller and, accordingly, makes A smaller (see Fig. 4). This theory is in accordance with the EPP theory. The choke point is the equivalent of the juncture of upstream and FLS according to EPP theory. Wave speed theory supplements EPP theory by addressing pressure-area relationships at the choke point and predicting values of maximal flow.

The EPP and wave speed theories and experiments support the concept that upstream and downstream segments are connected by a discrete airway segment, the choke point, which dissipates all increases in driving pressure and limits flow. Clinical application of these concepts improves our understanding of the impact of structural wall changes on flow dynamics in disease processes. For example, chronic inflammation and remodeling in asthma affect mechanical properties of the airway wall. Using esophageal balloons to measure pleural pressure and airway pressure probes, airway compliance can be determined at multiple anatomic points. Long-lasting asthma was found to cause less compliant central airways, suggesting that chronic inflammation and remodeling of the airway wall may result in stiffer dynamic elastic properties of the asthmatic airway.

**Applied Physiology**

**EPP theory and wave speed theory explain EDAC during forced expiration in healthy individuals**

The flow-limitation theories show that increasing pleural pressures during forced expiration result in greater dynamic airway compression downstream from the EPP and adjacent choke points. Clinical studies show sex and age differences in the degree of dynamic collapse. Dynamic CT investigations showed that regardless of age, men tend to have greater inspiratory and expiratory force-generating capacity. Maximum expiratory pressure is 30% to 50% greater among men compared with women throughout adulthood. If the effort is maintained throughout expiration, greater compression of the downstream airway segment might be expected in men than in women. Although the mean % collapse is similar for men (55% ± 23%) and women (52% ± 17%), only men (older men had both greater CSA at TLC and smaller CSA during dynamic exhalation than younger men) showed a significant positive correlation between % collapse and age. However, both sexes showed % collapse of more than 50% in healthy individuals. These results suggest that sex and age differences should be considered when assessing patients for suspected pathologic collapse and support the fact that the 50% cutoff for defining abnormality results in false-positive findings without consequence on flow.

**EPP theory and wave speed theory explain EDAC in COPD**

Two abnormalities in COPD contribute to early AC during expiration: decreased elastic recoil at all lung volumes (emphysema) and inflammatory narrowing of the airways (bronchitis). These processes determine the major site of increased resistance to be in the small airways (ie, airways of <2 mm diameter). In the presence of small airway obstruction, EPP and the choke points were shown to be further upstream (toward the alveoli) than in normal individuals. The destruction of lung tissue decreases the number and elasticity of the radial attachments from the parenchyma to the airway, and thus decreases airway stability. Experimental studies applying wave speed theory in canine models of emphysema show that the main reduction in maximum flow is explained by the decrease in elastic recoil; the other contributing factors are increases in frictional resistance from alveoli to sublobar bronchi and changes in airway compliance. A decrease in airway stability in emphysema decreases the maximum flow by decreasing CSA for a given transmural airway pressure, and by relatively increasing airway compliance. Alternatively, altered bronchial pressure-area behavior could result from a relative increase in peribronchial interstitial pressure. Thus, for a given intraluminal pressure P_l, airway CSA in emphysema would be smaller than in healthy lungs, because the transmural pressure (P_l–peribronchial pressure) would be less (see Fig. 4). This reduction in CSA in COPD has not been proved to be caused by cartilage abnormalities and thus cannot be considered true malacia. Physiologic and morphologic studies of determinants of maximal expiratory flow in COPD show that airway collapsibility did not correlate with the amount of airway cartilage, inflammation, or airway wall thickness. Decreased cartilage volume in COPD has been described by several investigators but was not found by others. Because the mechanical properties of airway cartilage have not been investigated, it cannot be excluded that these properties would relate in airway collapsibility. Some investigators reported that the proteolytic enzyme, papain, could weaken airway cartilage.
but not destroy it, because its histologic appearance remained unchanged.

A clinical study addressed the question whether expiratory flow limitation is caused primarily by narrowing of the central airways or by the more peripheral airways in patients who have COPD and concurrent abnormal degrees of central AC. The investigators analyzed the degree of central airway collapsibility by using a semiquantitative analysis of bronchoscopic images and related it to expiratory flow limitation in patients with what the investigators named TBM. However, all patients had invagination of the posterior membranous portion, which caused tracheal narrowing; the tracheal collapse was not caused by softening of the cartilaginous rings, thus making the entity studied consistent with a diagnosis of EDAC. Simultaneous pressure measurements in the trachea and esophagus were performed to identify expiratory flow limitation during quiet breathing and to determine the critical transmural pressure required for maximum expiratory flow. The investigators found that 15% of patients with EDAC were not flow limited during quiet breathing, 53% were flow limited throughout exhalation, and 30% were flow limited only during the latter part of the exhalation. Patients with flow limitation at rest had more tracheal narrowing (EDAC) than those without, but the severity of expiratory flow limitation was not closely related to tracheal collapsibility. AC during quiet breathing was unrelated to FEV₁ (forced expiratory volume in first second of expiration). Twenty-three patients (28%) were flow limited during quiet exhalation at transmural pressures that did not cause central AC. In these patients, the tracheal collapse was less than 50% during quiet exhalation and increased to more than 50% only during forced exhalation, when the pleural pressures increased, suggesting that tracheal collapse to more than 50% narrowing during forced exhalation is not responsible for limiting maximum expiratory flow. The important finding of this study was that EDAC was mostly seen in patients with tidal expiratory flow limitation. These data are relevant when considering interventions addressing EDAC, especially if symptomatic central airway narrowing exists without significant documented airflow obstruction. It could be argued that even in patients with EDAC during tidal exhalation, given the expiratory flow limitation at rest, EDAC represents the airway downstream (mouthward) from the choke points and is not responsible for pressure decrease and flow limitation. The way to show whether EDAC is flow limiting is to measure the degree of pressure decrease along the collapsing segment. However, the success of stent insertion or tracheoplasty is assessed not just by improvement in airflow but also by relief of symptoms such as cough and dyspnea and reduced frequency of infection. This finding is especially relevant for those patients with central AC in which collapse of the posterior membrane is noted and there is concurrent collapse of the cartilaginous wall, namely those patients with crescent-type malacia or a combination of malacia and EDAC. For this purpose, the use of intraluminal airway pressure catheter measurements distal and proximal to the narrowed airway during tidal breathing allows intraoperative estimation of the physiologic benefits of a particular interventional procedure.

The evidence that the degree of central AC in COPD is independent of disease severity and does not correlate significantly with physiologic parameters is reproducible. Dynamic CT studies suggest that the incidental identification of excessive expiratory tracheal collapse (measured at 1 cm above the aortic arch [midthrachea] and 1 cm above the carina [lower trachea]) in COPD is not clinically significant. One study evaluated 100 adults meeting GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria for COPD who underwent PFT, 6-minute walk test (6MWT), Saint George’s Respiratory Questionnaire (SGRQ), and spirometry gated low-dose CT at TLC and during dynamic exhalation with spirometric monitoring (CT was performed during a forced expiratory maneuver: participants took a deep breath and then blew out hard and fast [similar to a forced vital capacity [FVC] maneuver in the PFT laboratory]). The mean FEV₁ was 64% predicted, and percentage expiratory collapse was 59% ± 19% for tracheal measurement and 61 ± 18% for lower tracheal measurements. Twenty percent of the study participants met study criteria for excessive expiratory collapse, which was defined as a reduction of more than 80% in the tracheal lumen during forced expiration. Consistent with the bronchoscopic study described earlier, there was no significant correlation between percentage expiratory tracheal collapse and pulmonary function measures, total SGRQ score, or 6MWT distance. The SGRQ symptom subscale was only weakly correlated with percentage collapse of the midtrachea (R = 0.215, P = .03).

Bronchoscopic and dynamic CT studies highlight the fact that clinically significant EDAC that interferes with flow or symptoms should not be defined by forced expiratory maneuvers. The lack of association between the severity of tracheal collapse and GOLD stage of COPD was also described by other investigators, who
studied 71 patients with COPD, but these latter investigators reported a higher prevalence of excessive expiratory tracheal collapse (53%), likely because they used a lower threshold for diagnosis (>50%). Thus, the incidental detection of excessive expiratory tracheal collapse in a population with COPD of different degrees of airflow obstruction may not be clinically relevant, especially in the absence of other comorbidities. The resistance of the upstream segment based on EPP theory affects flow and determines the location of the choke points and the downstream compressed airway segment. From a clinical standpoint, severity of bronchial wall thickness, responsible for increased Resistance of the upstream segment (Rus), was significantly higher in patients with EDAC and correlated with the degree of maximal AC. Based on the mechanisms of flow limitation outlined earlier, central AC is a consequence of:

1. Increased pleural pressures, as seen during forceful expiratory maneuver or cough
2. Hypercompliant central airway during expiration, with relatively low pleural pressures, as seen with weakened or destroyed cartilage (TBM) or decreased drive pressure in the setting of peripheral airway obstruction (EDAC in COPD)
3. Increased resistance in the segment upstream from the choke point, as seen in chronic bronchitis, asthma, and bronchiectasis, which leads to EDAC
4. Decreased elastic recoil and early formation of choke points at high lung volumes during exhalation responsible for EDAC in emphysema

Such central AC could occur in patients with or without COPD, may not be flow limiting, and possibly not associated with impaired functional status. From a flow dynamic perspective, detection of expiratory tracheal or mainstem bronchial collapse at the level of the posterior membrane should trigger a search for causes of airflow obstruction within the lung (COPD, bronchiolitis, asthma), not the central airways.

EPP theory and wave speed theory explain EDAC in obesity

Obesity can cause low lung volumes and restrictive ventilatory impairment. Individuals with a body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters) greater than 40 kg/m² have reduced TLC, functional residual capacity (FRC), and vital capacity. In otherwise healthy obese individuals with BMI greater than 40 kg/m², expiratory flow limitation is common in the supine position.

Pleural pressure in obese individuals at relaxation volume is greater than normal, often becoming positive. This finding was shown in obese supine and paralyzed individuals undergoing general anesthesia and also in conscious obese individuals. Based on the EPP theory, the increased pleural pressure throughout the chest in these individuals explains the EDAC that is often encountered during bronchoscopy or dynamic CT, because transmural pressure (Pₐ–Ppl) is decreased, and during exhalation the airway collapses at the posterior membrane portion, causing EDAC (see Fig. 4).

Pathophysiology: key points

1. Healthy volunteers performing forced expiratory maneuvers and patients with morbid obesity, COPD, and other obstructive ventilatory disorders have EDAC as a result of interactions between pleural pressures, elastic recoil, airway compliance, and peripheral airway resistance.
2. EDAC documented on bronchoscopy or dynamic CT may not interfere with flow, regardless of the degree of AC.
3. EDAC may not correlate with severity of ventilatory impairment or QOL measures.

FUNCTIONAL EVALUATION

Pulmonary Function Testing

Spirometry in patients with central AC may reveal obstructive ventilatory impairment but does not correlate with severity of the airway narrowing. Spirometry measurements are not necessarily representative of the degree of symptomatic improvement after interventions such as stent insertion or tracheoplasty, suggesting that interventions either improve other factors (cough, secretion management) or do improve pulmonary mechanics but not airflow as measured by FEV₁% predicted. However, the flow-volume curve contour in COPD correlates with pulmonary mechanics, and 2 different types of flow-volume loops are identified: AC and scoped-out patterns (Fig. 5). AC pattern is characterized by a decrease in flow rate from the peak flow to an inflection point less than 50% of peak flow rate. The inflection point occurs within the first 25% of expired vital capacity. The inspiratory limb of the curve showing no evidence of obstruction can be seen in almost 40% of patients with COPD, and it correlates with the bronchoscopic finding of EDAC. The groups of patients with the 2 distinct flow-volume
loops patterns cannot be distinguished from clinical symptoms.\textsuperscript{55} Results of studies show higher resistance to flow in AC group at high and mid lung volumes but comparable resistance to flow at lower lung volumes in both groups. The RV and FRC were higher in the AC group, indicating a more severe hyperinflation, despite comparable loss of elastic recoil, consistent with functional closure of small airways caused by intrinsic airway abnormality. The degree of hyperinflation was found to have no correlation with the peak flow or the flow rate at the inflection point in the AC group. At the peak flow, the mean pleural pressure was similar in the 2 groups; below peak, the AC group had considerably higher maximal pressure compared with the non-AC group, and this was sustained through 75\% of expired vital capacity. These data suggest that AC pattern seems to be determined by a combination of loss of elastic recoil and peripheral AC, findings supporting the EPP theory. Flow oscillations on the flow-volume loop have also been described in patients with ECAC. These oscillations take on a saw-tooth appearance, defined as a reproducible sequence of alternating decelerations and accelerations of flow.\textsuperscript{56}

Impulse oscillometry (IOS) is an effort-independent test during which brief pressure pulses generated by a loudspeaker mounted in series with a pneumotachygraph are applied during tidal respiration, and recordings are used to provide an estimate of total respiratory system impedance. Measurements of resistance (R) and reactance (X) at different frequencies might differentiate between central and peripheral components of airway obstruction. Increased R at a low oscillation frequency (5 Hz) reflects an increase in total respiratory resistance suggestive of airway obstruction such as that found in patients with COPD, whereas an increase at a higher frequency (20 Hz) reflects more specifically increased central airway resistance such as that found in patients with central airway obstruction.\textsuperscript{57} The IOS maneuver does not cause respiratory fatigue and may be better tolerated by patients with irritable, inflamed airways such as those with ECAC. However, preliminary reports suggest that IOS data from ECAC are similar to those from patients with COPD, resulting in increased resistance at 5 Hz, marked frequency dependence in resistance, more negative reactance at 5 Hz, and increased resonant frequency.\textsuperscript{58} Normalization or improvement of IOS data after treatment of ECAC confirms that the IOS pattern is caused by the central AC and not peripheral obstruction.\textsuperscript{58} Furthermore, because in EDAC the predominant site of flow limitation is in the periphery, higher R5 and R5 to R20 values are expected than with TBM, for which the main site for flow limitation is the central airways, and thus higher R20 is expected. These findings need to be confirmed in future studies.

![Flow-volume loop patterns in COPD. (A) The AC pattern shows a sudden decrease in peak expiratory flow, defined as a 50% decrease within 25% of FVC. (B) The scooped-out pattern is without an initial spike and is characterized by a more curvilinear reduction in flow rate over the vital capacity.](image)
**Functional Bronchoscopy**

Functional bronchoscopy consists of physiologic measurements during bronchoscopy and performance of dynamic bronchoscopy. This latter technique refers to bronchoscopy performed during various respiratory maneuvers with the patient having received at most only anxiolytics. The patient can thus follow commands and cooperate during the procedure with respiratory maneuvers and changes in body position. For instance, a patient with malacia and orthopnea may not have the bronchoscopic findings of malacia unless the bronchoscopy is performed in a supine position. Similarly, a patient with a history of tracheostomy and dyspnea when bending over or during neck flexion may have posttracheostomy stomal structure, with malacia revealed only when the lesion becomes intrathoracic and increased pleural pressures during exhalation result in further narrowing of the airway lumen and cause flow limitation, inability to raise secretions, or trigger coughing spasms. Conversely, if the lesion is at the thoracic inlet, symptoms may occur only during inspiration if the lesion becomes extrathoracic, such as when the patient performs neck extension.

Intraluminal pressure, changes in pressure over the length of a stenosis, and airflow can be superimposed over the bronchoscopic image in real time using a technique of endspirometry. Dynamic changes can be studied during quiet breathing, forced breathing maneuvers, coughing, and neck flexion/extension, and the impact on pressure change responsible for symptoms can be determined. Results from studies show that intraluminal pressure monitoring allows the detection of the FLS responsible for flow limitation. With the use of airway catheters in dogs and in humans, the FLS could be located by measuring airway pressure (PL) during induced flow limitation generated by either an increase in pleural pressure or a decrease in downstream pressure.

Because assessment of the FLS requires forced expiratory vital capacity maneuvers, detecting flow limitation by measuring PL cannot be performed during bronchoscopy if patients cannot follow instructions, such as those patients undergoing general anesthesia. However, a simple and well-tolerated bronchoscopic technique has been proposed and studied in this setting, using PL measurements: a double-lumen airway catheter capable of simultaneously measuring PL at 2 sites in the trachea can be used to assess tracheal obstruction. When the catheter is positioned with the 2 holes located on each side of a stenosis, the 2 pressures plotted against each other show a line with a slope less than 45° caused by resistance difference between the 2 points. If the 2 holes are simultaneously located proximal from or distal to the narrowing, pressures between these sites are in phase, and if plotted against each other, show a straight line with a slope of 45°. By measuring airway pressure proximal and distal to the narrow airway segment and plotting the 2 pressures against each other during quiet tidal breathing, the site of maximum obstruction and the degree of narrowing can be physiologically assessed, allowing intraoperative prediction of the procedural outcomes.

Bronchoscopy allows direct visualization of the airway mucosa, can be performed in critically ill patients at the bedside, is not associated with ionizing radiation, and allows assessment of response to noninvasive positive pressure ventilation (NIPPV) when this is considered a treatment alternative. For this purpose, a full face mask can be used and secured to the patient’s face with elastic straps. A dual-axis swivel adapter (T-adapter) is also attached to the mask and connected to the ventilator. NIPPV is applied in incremental pressures until the AC is palliated or until the patient becomes uncomfortable (patients have occasionally reported chest tightness, dyspnea, and uncomfortable pressure sensation over the face and choking during bronchoscopic continuous positive airway pressure [CPAP] titration for ECAC), whichever comes first. A CPAP pressure of 0 cm H2O is usually initiated and titrated upwards. If necessary, as in the evaluation of central AC, procedures are performed in the upright and supine positions as well as on and off CPAP to evaluate the degree of airway narrowing and response to CPAP (Fig. 6). In EDAC/TBM, CPAP pressures of 7 to 10 cm H2O usually assure airway patency but pressures can be increased by 3 cm H2O incrementally until airway caliber during tidal exhalation is considered satisfactory (eg, at least 50% of that noted during inspiration). Intraluminal pressure monitoring during CPAP is possible (Lutz Freitag, MD, Germany, personal communication, 2012) but has not yet been systematically studied.

**Dynamic CT**

Low-dose dynamic CT reveals TBM and EDAC when performed according to a central airway protocol, which includes end-inspiratory and dynamic-expiratory imaging. Scout images are captured to determine the area of coverage (trachea, mainstem bronchi, and bronchus intermedius). Scanning is performed in a craniocaudal
direction during both end-expiratory and dynamic-expiratory phases, and the percentage of AC is calculated by subtracting the dynamic-expiratory CSA from the end-inspiratory CSA, divided by the end-inspiratory CSA. Some protocols capture images at 3 different time points during the respiratory cycle: at the end of inspiration, at the end of expiration, and during dynamic exhalation.\(^6^3\)–\(^6^5\)

The use of end-inspiratory CT images alone is not useful for detecting TBM or EDAC, because after closing the vocal cords for a breath-hold, the intraluminal airway pressure can become positive, the transmural pressure increased and the airways can be distended. End-expiratory CT images at suspended exhalation may also be misleading for similar reasons; the intraluminal pressure may be higher than during dynamic expiration, and because the expiratory effort has ceased, the pleural pressure is not maximal and the degree of collapse may be diminished. End-expiratory CT images at suspended exhalation accentuates AC because images are captured during forced expiratory maneuver, not tidal expiration. The abnormal collapse detected does not reflect the patient’s airway dynamics during tidal respiration. In addition to showing potentially a nonpathologic process and causing false-positive diagnosis, dynamic CT also requires additional technologist training. Supervision and coaching of patients is necessary, not always feasible in very dyspneic, uncooperative, or critically ill patients. If patients start coughing, the degree of AC is accentuated even further.\(^6^6\) Three-dimensional reconstruction images are useful for obtaining a perspective on the extent and degree of collapse, but the axial images are used for accurate measurements of CSA. In general, 3 anatomic levels for each respiratory cycle time point are examined (the aortic arch, main carina, and intermediate bronchus), but there is inconsistency among studies in regards to the number and location of anatomic sites chosen for airway lumen measurements.\(^6^,7,11,12,6^3\)–\(^6^7\)

Dynamic CT was shown to reveal similar degree of AC to bronchoscopy.\(^6^3,6^8\) Given its noninvasiveness, dynamic CT can be used as the initial test when TBM or EDAC is suspected. However, most investigators use dynamic CT as an adjunct not an alternative to bronchoscopy in preoperative
planning or posttherapy monitoring. CT measurements of forced expiratory tracheal collapse are highly reproducible over time and thus can be used for monitoring after intervention and progression of disease. Dynamic CT has been used for general preoperative imaging to assess the degree of narrowing and craniocaudal extent of AC, to define intrinsic (eg, cartilage thickening in relapsing polychondritis) or extrinsic (eg, compression by mediastinal masses or vascular structures) abnormalities and to plan stent insertion by allowing measurement of the airway caliber. CT has been used to follow up patients after stent placement to assess stent patency, detect complications such as migration, formation of granulation tissue, mucus obstruction, or choke point migration. CT was also used in the preoperative evaluations of patients being considered for tracheoplasty to confirm extent, severity, and airway shape because patients with crescent-type TBM are most likely to benefit from reinforcement of the posterior membrane. CT allows exclusion of other diseases requiring different interventions, such as a paratracheal mass or relapsing polychondritis. Postoperative evaluation after tracheoplasty can be performed using CT, which reveals changes in the degree of expiratory collapse and potentially detects the rare but severe complications of this procedure, such as airway dehiscence, mediastinal hematoma, or abscess.

In addition to noninvasiveness, the main advantage over bronchoscopy is the ability to evaluate the structures around the airways potentially responsible for malacia (ie, goiter, aortic aneurysm, double aortic arch) and assess the changes of lung parenchyma that may cause or be associated with central AC (ie, emphysema, bronchiolitis, air trapping). The disadvantages include the lack of details about the mucosa, the necessary patient cooperation with respiratory maneuvers, and exposure to ionizing radiation. Lower-dose techniques allow a 23% radiation dose reduction compared with the standard technique. These techniques can be used for central airway imaging because of the inherent contrast between central airways and adjacent soft tissue without compromising diagnostic information. Advances in CT technology allow now faster image acquisition. The 320-detector row scanner covers 16 cm craniocaudal volume per rotation and allows real-time dynamic imaging of trachea. This technique has already been used for diagnosis of EDAC and assessment of response to CPAP.

However, from a physiologic standpoint, dynamic CT findings of excessive AC during forced exhalation have been considered of uncertain physiologic significance. Recent dynamic CT studies are in agreement with the physiologic understanding of EDAC based on the flow-limitation theories. Although the previous definition of abnormal collapse greater than 50% cross-sectional luminal collapse is still used by investigators, symptomatic collapse, which may require interventions, is usually 95% to 100%. Advances in imaging resulted in changing of our understanding of the pathologic central AC. Initial radiographic definition of cross-sectional diameter reduction of 50% or greater during coughing on bronchography dating from more than 45 years ago is now known to be inadequate because 80% of normal healthy individuals meet this criterion during forced exhalation. The different degrees of AC noted on imaging studies led to radiologic subtyping of the 50% or greater criterion according to severity. Results of studies show that the % expiratory decrease in CSA should not be the only criterion, because there is overlap in degree of expiratory collapse among healthy volunteers and patients with central airway disease, furthermore, the degree of collapse greater than 50% is not uncommon in COPD and may not be responsible for flow limitation.

Results of studies show the presence of the highly collapsed central airways in COPD using dynamic-expiratory or end-expiratory CT scans and the lack of significant physiologic impairment resulting from EDAC. For instance, one study aimed to reveal the correlations between tracheal volumetric measures, including collapsibility, and lung volume measures on inspiratory and end-expiratory CT scans to evaluate the relationship between tracheal collapsibility and lung function. The study included 85 smokers (normal lung function [n = 14]; GOLD stage 1 [n = 14]; stage 2 [n = 36]; stage 3 [n = 11]; stage 4 [n = 8]) who underwent PFTs and chest CT at full inspiration and end-expiration. Tracheal volume and collapsibility, expressed as expiratory/inspiratory (E/I) ratios of these volumes, were found to be related to lung volume and collapsibility. The highly collapsed trachea on end-expiratory CT did not indicate more severe airflow limitation or air trapping in smokers because only weak correlation was found with FEV1/FVC or RV/TLC ratios, respectively. The tracheal collapsibility negatively correlated with FEV1/FVC and FEV1% predicted, suggesting that the highly collapsed trachea on end-expiratory scans indicated less severe airflow limitation in the individuals analyzed in this study. These findings add to the body of evidence that the collapsed trachea on end-expiratory scans in the form of EDAC is not a morbid finding and should be distinguished from the abnormally collapsed trachea in TBM.
These observations are relevant for future radiologic and physiologic studies of tracheal collapse in COPD or TBM. In addition to COPD, using dynamic CT, EDAC was also shown in 69% adult patients with cystic fibrosis. Based on data from dynamic CT studies, radiology literature suggests the need for more rigorous criteria for diagnosing clinically relevant EDAC, with potentially separate diagnostic threshold levels for the trachea and right and left bronchi. Correlation of forced expiratory CT findings of EDAC with symptoms and pulmonary function testing is necessary in the decision-making process before considering EDAC a cause of a patient’s symptoms and subsequently proceed with interventions.

The increasing use of dynamic CT for TBM and EDAC led to recognition of several morphologic types of central AC. Similar to bronchoscopic classifications, numerous descriptive terms have been proposed, but no 1 system has been universally adopted. CT classification is based on morphology on inspiratory and expiratory images. For instance, on inspiratory images, the normal trachea is generally oval or round. In patients with the most common type of TBM (the crescent type), even during inspiration, the anterior wall of the cartilage is flattened and the shape of the trachea has been described on CT scans as lunate, in which the coronal/sagittal diameter ratio is greater than 1. A second type is the saber-sheath morphology, usually associated with COPD. Some patients with this type of tracheal configuration have malacia as well, but this can occur in the presence of normal inspiratory tracheal morphology. A biconvex, fish-mouth pattern has also been described. Based on expiratory images, the terms used in the radiology literature include crescent, characterized by marked anterior bowing of posterior wall, or the so-called frown sign and circumferential, characterized by isotropic reduction in airway cross section.

**Dynamic Magnetic Resonance Imaging**

The use of magnetic resonance imaging (MRI) has been rarely reported in adults with TBM and EDAC, but it is used to diagnose and monitor response to stabilization techniques for pediatric TBM. MRI studies reveal similar results with those from dynamic CT analyses of central AC. For instance, in 1 study, a significantly higher collapse was found in patients with COPD compared with volunteers, with 70% of patients with COPD showing a collapse of more than 50%. Contrary to CT scanning, MRI has the advantage of avoiding radiation and offering superior contrast resolution and more definitively characterizes soft tissue masses. MRI can delineate tracheal and main bronchial patency and their close anatomic relationship with the adjacent vascular structures. Modern MRI allows central airway imaging with adequate resolution. As with CT, contrast agents are still used, but in the case of MRI, intravenous gadolinium contrast-based agents are generally recommended unless contraindications exist. Images can be affected by respiratory and cardiac motion artifact, which makes interpretation of intrathoracic MRI images more difficult. Mainstem bronchi trajectories are oblique and bias the accuracy of CSA measurement. Increased acquisition times often require the patient to stay still for at least several minutes at a time, which may not be possible in dyspneic, uncooperative, or critically ill patients. The MRI examination takes about 15 minutes. Three dynamic measurements can be performed in the coronal, oblique, and transverse orientation, respectively. Minimal and maximal cross-sectional luminal diameters and tracheal lumen area can be calculated. In 1 study, the median degree of tracheal collapse was found to be 43% in volunteers and 64% in smokers. The maximal CSA of the upper tracheal lumen as well as the expiratory collapse was larger in patients with COPD than in normal individuals. Similar to data from CT studies, a significant proportion of patients with COPD (70%) and 30% of volunteers showed a collapse of more than 50%. Overall, however, the high spatial (submillimeter) and temporal resolution (10 frames/s) of dynamic CT cannot yet be obtained by MRI techniques.

MRI has been used to assess focal malacia associated with laryngotracheal stenosis or diffuse malacia from relapsing polychondritis. The dynamic (cine) MRI has been particularly useful to define pediatric TBM. MRI is established as the standard modality for imaging the pediatric mediastinal airway. Ventilation and perfusion mapping and quantification are also possible and may have a role in the future MR imaging of patients with TBM and EDAC.

**High-Frequency Endobronchial Ultrasoundography**

High-frequency endobronchial ultrasoundography (EBUS) using a 20-MHz radial scanning probe was shown to identify the hypoechoic and hyper-echoic layers that correlate with the laminar histologic structures of the central airways. Cartilage abnormalities (weakness, fracture, edema) was described in patients with malacia caused by tuberculosis, relapsing polychondritis, lung cancer, and compression by vascular rings.
EBUS could potentially distinguish between TBM and EDAC because in the latter it seems that the cartilage is intact, and the posterior membrane is thinner than normal, likely because of atrophy of elastic fibers. The instability of the posterior tracheal wall is in agreement with the known loss of elastic fibers, which enables inflation and collapse during respiration. Cartilage abnormalities in the central airways of patients with COPD and ECAC have not been systematically studied with EBUS. This finding is relevant because based on wave speed theory and EPP theory, the CSA at the choke point is determined by the pleural pressures, resistance of the upstream airways and compliance of the airway. It is relevant for treatment to know if the airway compliance is increased because of the reduced stiffness from weakened cartilage. However, the pathologic hallmarks of COPD are destruction of the lung parenchyma, which characterizes emphysema; inflammation of the peripheral airways, which characterizes bronchiolitis, and inflammation of the central airways, which characterizes chronic bronchitis. In patients with chronic bronchitis, inflammation was found to be present in the airway wall and in the mucous glands, particularly in cartilaginous bronchi larger than 2 mm in diameter. However, there is no mention of cartilaginous destruction in biopsy studies of patients with COPD. More studies are needed, but there is potential for high-frequency EBUS to be used as a surrogate of histology in patients with ECAC.

Vibration Resonance Imaging

Vibration response imaging (VRI) is a noninvasive imaging tool using piezoelectric sensors to transform analog signals from the chest into dynamic grayscale images similar to the process involved in ultrasound imaging. VRI has been reported in the evaluation of patients with asthma, COPD, aspiration of foreign objects, and central airway obstruction undergoing bronchoscopic interventions. The experience in patients with ECAC is limited, but the disappearance of floating and fluttering dynamic imaging pattern after stent insertion is consistent with previous studies showing improvement in patients with other forms of central airway obstruction after bronchoscopic interventions. Because sounds at frequencies of 100 to 250 Hz are mainly generated in the central airways and frequencies of 500 to 650 Hz in the terminal bronchioles, the differential analysis of VRI might allow localization of pathologic processes in different compartments of the lung. TBM and EDAC may provide different dynamic grayscale images, because in TBM, the FLS are predominantly central, whereas they are peripheral in EDAC, although these hypotheses remain to be studied. Given its noninvasiveness, this modality could potentially be used for telemedicine monitoring of symptomatic patients.

Evaluation: key points

1. Spirometry values do not correlate with the degree of AC.
2. Expiratory flow-volume curve may show a sudden decrease in peak flow very early during a forced expiratory maneuver (also known as AC pattern) or flow oscillation (also known as saw-tooth pattern).
3. Dynamic and functional bronchoscopy are performed to distinguish and classify TBM and EDAC, to determine choke point location, and subsequently to decide on the need for and type of treatment.
4. Low-dose paired inspiratory–dynamic-expiratory CT is complementary to bronchoscopy by providing information about the adjacent vasculature, mediastinal masses, or parenchymal changes that may explain the cause of ECAC.
5. Low-dose paired inspiratory–dynamic-expiratory CT results in false-positive findings of EDAC if the 50% cutoff is used to define abnormal collapse.
6. Dynamic MRI can be used to detect ECAC and has lower resolution than CT scanning but is preferred in the pediatric population because of lack of ionizing radiation.
7. High-frequency EBUS may be used as a surrogate of histology to identify structural airway wall changes in ECAC.

TREATMENT

Functional impairment attributable to ECAC warrants evaluation for treatment. Patients with incidental abnormal AC on bronchoscopy or CT scanning performed for other reasons should not undergo interventions. Functional impairment in ECAC may result from at least 3 causes: dyspnea, cough, mucus retention. EDAC is also associated with higher morbidity and poorer survival in elderly patients who have undergone bronchial and bronchovascular sleeve resections for lung cancer. Therefore, as for other pulmonary disorders, QOL and functional impairment scales may be appropriate to measure the impact of respiratory symptoms on overall health, daily
life, and perceived well-being in patients suffering from ECAC. This evaluation typically involves PFTs, 6MWT, and determination of Karnofsky performance status, American Thoracic Society Dyspnea Score, and respiratory-affected QOL based on the SGRQ.

Significant impairment of the patient’s functional status and QOL is necessary before considering potential intervention. However, there are no controlled studies to support 1 therapy versus another. Research is limited by ethical issues. For instance, a randomized trial of tracheobronchoplasty versus sham surgery is obviously not feasible, but it is possible to design a randomized study of rigid bronchoscopy and rigid bronchoscopy plus Y-stent placement for diffuse and severe EDAC. The disease process, before invasive interventions, has to be clearly defined and quantified in terms of morphology of ECAC, extent, severity of narrowing, and impact on functional class and QOL scores (Fig. 7).

**Cause-Based Treatment Strategies**

Treatment of the primary cause of AC may or may not improve the degree of airway narrowing or symptoms. The invasive nature of alternative strategies (stents, tracheoplasty) justifies an initial attempt at medical treatment of the cause of EDAC/TBM. For instance, reversibility of EDAC can occur after properly treating chronic bronchitis with bronchodilators, steroids, and antibiotics. In 1 study, the AC pattern on the flow-volume loop characterizing EDAC showed complete reversibility in a few (3/20) patients after 3 weeks. From a physiologic standpoint, based on EPP theory, this finding is relevant because the AC pattern can normalize after treating bronchitis (Rus component) without a concomitant normalization of elastic recoil. On the other hand, bronchodilators may increase airway wall compliance, suggesting that increased compressibility of the large airways causes the EPP to become fixed at a point nearer the thoracic outlet. The increased length of the upstream segment (Rus) and decreased CSA at the EPP would thus offset the advantage gained by increased caliber of upstream airways with respect to maximal expiratory flow rates. This finding may explain why some patients with EDAC caused by COPD do not improve after bronchodilators. Some patients may have worsened maximum expiratory flow rates.

Treatment of emphysema itself could lead to improvement in EDAC, further supporting the argument that EDAC is not a primary tracheobronchial disorder. Improvement in expiratory flows after lung volume reduction surgery is largely caused by increases in recoil pressure (Pst). Placement of the endobronchial valves results in less hyperinflation (improved Pst), and bronchoscopic follow-up may show improved EDAC (Hugo Oliveira, MD, Brazil, personal communication, 2008), but this hypothesis needs to be tested in emphysema treatment trials. For patients with a known cause of cartilage inflammation such as relapsing polychondritis, treatment with immunosuppressive therapy is offered first unless the airway is critically narrowed and the patient in extremis (see Fig. 7). However, results of studies and clinical experience suggest that once malacia has developed, antiinflammatory agents may not restore cartilage integrity. For patients with disease refractory to medical treatment, strategies aimed at restoring airway patency are offered based on the degree of airway narrowing, cranio-caudal extent, and, most importantly, impact on symptoms, predicted response, and expected complications (see Fig. 7).

**NIPPV**

Application of positive airway pressure serves as a pneumatic stent because the intraluminal pressure is increased, thus improving the airway stiffness and expiratory flow based on wave speed theory (Equation 2). Alternatively, flow may be improved simply because lung volumes are higher during positive pressure ventilation. The higher elastic recoil, based on the EPP theory, improves the maximum expiratory flow (Equation 1). Data from pediatric TBM confirm this concept. CPAP significantly increased maximal expiratory flow at FRC in healthy infants and infants with tracheomalacia. This increase in flow at FRC was secondary to the increase in lung volume with CPAP, because maximal expiratory flows measured at the different levels of CPAP were not different when compared at the same lung volumes. The optimal level of CPAP in infants with severe tracheomalacia may be related to increasing the lung volume to a level at which the infant is not flow limited during tidal breathing, without also significantly increasing the work of breathing through a decrease in pulmonary compliance at increased lung volumes.

From a clinical standpoint, regardless of its mechanism of action, CPAP was shown to improve dyspnea, cough, and secretion management in selected patients with TBM. The amount of pressure necessary to maintain airway patency can be determined by performing bronchoscopy assisted by NIPPV. Adjunctive NIPPV decreases pulmonary resistance and can be used to improve spirometry values, sputum production,
atelectasis, and exercise tolerance, but its long-term efficiency has not been clearly shown.\textsuperscript{23,109,110} NIPPV has been used in adults with TBM from relapsing polychondritis and tracheomalacia from long-standing compression by a large goiter or thyroid cancer, wherein the cartilaginous rings of the trachea are considerably weakened or destroyed, leading to softening and floppiness of the trachea. NIPPV was also effective and safe in the management of stridor and airway compromise after early extubation of patients with postthyroidectomy tracheomalacia.\textsuperscript{111} In 1 study, 6 patients developed stridor and airway compromise, which resolved immediately with the initiation of NIPPV without further respiratory support being required and without complications.\textsuperscript{111}

Application of noninvasive positive expiratory pressure (PEP) may improve expiratory flow and cough efficiency in patients with ECAC. This finding was shown in a study of 40 children with TBM.\textsuperscript{112} Patients and 21 age-matched controls performed spirometry followed by cough spirometry with PEP of 0, 5, 10, 15, and 20 cm H\textsubscript{2}O using an adjustable PEP valve. Cough expiratory flow between 75% and 25% of vital capacity (CEF\textsubscript{25-75}) for each curve was calculated to represent the effectiveness of cough at midlung volume. In the TBM group, CEF\textsubscript{25-75} increased by a mean of 18.8%, 1.7%, and 0.5% at PEP of 5, 10, and 15 cm H\textsubscript{2}O, respectively, but decreased by 2.4% at PEP of 20 cm H\textsubscript{2}O. In the control group, the CEF\textsubscript{25-75} decreased at all levels of PEP, with worse flow at higher PEP levels.\textsuperscript{112} This study\textsuperscript{112} suggests that the use of adjustable PEP valve increases flow during cough spirometry and may provide a useful adjunct to chest physiotherapy. It also shows the importance of scientifically choosing PEP levels, because higher levels (ie, 20 cm H\textsubscript{2}O) may worsen expiratory flow.

**Bronchoscopic Interventions**

Some patients with EDAC improve QOL after insertion of a central airway stabilization by stent. However, this situation is not explained by improvement in airflow as measured by FEV\textsubscript{1}.\textsuperscript{53} One explanation for improved symptoms is that central airway stability makes the flow less turbulent, similar to heliox, which was shown to improve exercise capacity in patients with moderate to severe COPD.\textsuperscript{113} In the short-term (10–14 days), airway stabilization using silicone stents in patients with various forms of ECAC was shown to improve respiratory symptoms, QOL, and functional status.\textsuperscript{53,114} In 1 large study, 45 of 58 patients (77%) reported symptomatic improvement; QOL scores improved in 19 of 27 patients (70%); dyspnea scores improved in 22 of 24 patients (91%); and functional status scores improved in 18 of 26 patients (70%).\textsuperscript{53} Stents may also improve outcomes for patients with Mounier-Kuhn syndrome\textsuperscript{115} and have been used in patients with malacia from relapsing polychondritis, with variable results.\textsuperscript{39,116,117} Of 8 patients with bronchoscopically detected TBM in a study of patients with relapsing polychondritis, only 3 were treated (2 by stent insertion and 1 by tracheostomy and removal of previously placed stents).\textsuperscript{118} Metal stents have been used in the past with variable success in patients with TBM. Advantages include placement by flexible bronchoscopy, dynamic expansion, and maintenance of airway mucociliary function with uncovered stents. However, in some studies, metal stents had to be removed because of stent mechanical failure or because of stent-related complications. Stent fracture and fatal hemorrhage from perforation have been reported; in the United States, metal stents are no longer recommended for use in benign central airway disease if other alternatives are available.\textsuperscript{119,120}

To potentially detect stent-related adverse effects or migrated choke points requiring further interventions, follow-up bronchoscopy or dynamic CT has been used in clinical studies.\textsuperscript{121} Stent-related adverse events are common and usually occur within the first few weeks after stent insertion (median time 4 weeks).\textsuperscript{53,114} These results seem to justify follow-up imaging 4 to 6 weeks after stent insertion (see Fig. 7). Sometimes, follow-up detects distally migrated choke points after stent insertion.\textsuperscript{39,40} Placing a stent at the site of maximal collapse during exhalation might result in migration of the choke point toward the periphery of the lung\textsuperscript{122} and has been addressed in patients with central airway obstruction caused by lung cancer and also in patients with malacia from relapsing polychondritis. Additional stents may be required if patients are still symptomatic and the choke points are still in the central airways. In 1 series, bilevel positive airway pressure was used after stent insertion for patients whose choke points had migrated to the small bronchi, as documented on CT.\textsuperscript{39} Rather than inserting more foreign material into an already inflamed airway, it may be more reasonable to use adjuvant NIPPV. If stent insertion does not improve symptoms and there is no migration of the choke points, then stent removal is advisable to avoid complications. Stent migration, obstruction by mucus and granulation tissue, infection, fracture, and airway perforation are well described in the literature.\textsuperscript{3} The distinction between stent-related adverse events and symptoms related to TBM may be difficult to assess based on clinical grounds, so any new
onset or worsening of symptoms should prompt bronchoscopy or CT scanning (see Fig. 7).
Yttrium aluminum perovskite (YAP) laser treatment has been anecdotally reported to improve lung function and symptoms in EDAC caused by Mounier-Kuhn syndrome; laser was applied with the intention of stiffening the posterior membrane by devascularization and subsequent...

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**ECAC identified on**
- Paired inspiratory-dynamic expiratory CT
- and/or
- Dynamic bronchoscopy

**Pulmonary function tests**
- Assess etiology and morphology
  - (TBM or EDAC)
- Quantify extent and degree of airway narrowing and functional class

**Treat underlying disease process**
- Pulmonary hygiene (chest physiotherapy, mucolytics, adjustable PEP valve)

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**Bronchoscopy on NIPPV**
- Determine the settings that maintain airway patency and are well tolerated by the patient

**Functional bronchoscopy to determine FLS**
- FLS in the trachea and/or mainstem bronchi
  - Yes
  - Stent insertion
  - +
  - Permanent stent
  - -
  - Remove stent
  - Dynamic bronchoscopy/dynamic CT for detecting stent migration, granulation, obstruction by mucus or migrated choke points

- No
- No tracheoplasty
- Search for alternative explanations for patient’s symptoms

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**Prescribe NIPPV at night and intermittently during the day for symptoms of inability to clear secretions, severe coughing spasms and increased dyspnea**

**Follow up H&P and PFTs, dynamic CT and/or bronchoscopy in case of symptoms recurrence**

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For critically ill patients
retraction of tissues.123 Its wavelength is double that of the yttrium aluminum garnet laser, allowing for tissue devascularization and coagulation at low power (15–20 W) in a discontinuous mode.124 The depth of penetration using YAP laser is estimated at 3 mm and may reach the submucosal tissues, triggering a fibrotic process125 that may stiffen the posterior membrane. Concerns remain about posterior membrane perforation and relapse of disease with the need for repeated interventions.

**Surgical Interventions**

Cervical tracheoplasty, resection/reconstruction, or tracheostomies are usually performed for extrathoracic tracheal malacia. Tracheal resection has been proposed for focal tracheomalacia, with good outcome and low mortality in experienced centers.126 However, this procedure was performed for posttracheostomy-related malacia and not for extensive disease. Open surgical interventions for intrathoracic disease include airway splinting and tracheostomy. Splinting (tracheoplasty) has been used to consolidate and reshape the airway wall, whereas tracheostomy is performed to maintain a stable airway and potentially bypass the malacic segment. Tracheostomy provides invasive ventilatory support if necessary, but it can be complicated by secondary tracheomalacia and stenosis and should not be considered a first-line treatment in elective cases. Before proposing membranous tracheoplasty, a stent trial has been used to identify those patients who are likely to benefit from surgery in the long term. When performed on this protocol, membranous tracheoplasty seemed to provide a favorable outcome in uncontrolled studies.

This procedure reinforces the membranous portion of the trachea in severe diffuse ECAC.54,127 The thoracic airways are splinted from the thoracic inlet to the distal left mainstem bronchus and distal bronchus intermedius. The outcomes of membranous tracheoplasty are promising, but complications are not insignificant; for instance, 1 study evaluated 66 patients with severe diffuse crescent-type TBM and EDAC (disease affecting trachea and bilateral mainstem bronchi).128 However, the 2 entities were grouped together under TBM and results were not reported separately. Thirty-seven patients had complete sets of preoperative and postoperative measurements of FEV1, and no significant difference was shown before and after the procedure. Twenty-two of 37 patients had improved FEV1, with a mean increase of 234 mL, whereas 15 of 37 patients showed no improvement or frank worsening of their postoperative FEV1, with a mean decrease of 235 mL, and 1 patient also had the same FEV1 values preoperatively and postoperatively. This study confirms earlier physiologic findings that stabilization of the collapsing tracheal and bronchial airway may not improve airflow but may result in improvements in short-term (3-month) QOL measurements. The median length of stay in the hospital after this surgical intervention was

Fig. 7. Management algorithm for diffuse ECAC. Once identified on dynamic CT or dynamic bronchoscopy, PFTs are performed (if not performed previously) to assess if there is any associated impact on maximum expiratory flow or dynamic hyperinflation. A clear categorization as TBM or EDAC is performed and cause is searched for. The extent, degree of narrowing, and impact on functional status and QOL are then evaluated to determine if treatment is warranted. The cause of the process (when known) should be medically treated first, if possible.
In addition to disease-specific treatment, chest physiotherapy, mucolytics, adjustable positive expiratory pressure valves can be used to improve secretion management. If the underlying cause is treated and the patient improves, a follow-up strategy with clinical examination, PFTs, and CT/bronchoscopy is warranted in case of symptom recurrence. If this fails and the patient is critically ill (unable to be weaned from invasive or noninvasive ventilatory support), the airway has to be stabilized and stent insertion is performed. If the patient is not critically ill, then NIPPV-assisted bronchoscopy is performed to determine if positive pressure application maintains airway patency. If the airway patency is maintained during NIPPV application, then those particular settings can be prescribed for nighttime NIPPV and intermittent use during the day as triggered by symptoms. If the patient does not respond to NIPPV, 1 strategy involves a so-called stent trial. If there is improvement (objectively documented), tracheoplasty is offered to operable patients; if patients are not surgical candidates, a permanent stent insertion is an alternative understanding if there is a high risk for stent-related adverse effects. Alternatively, functional bronchoscopy can be performed to localize the FLS amenable to stabilization techniques (stent insertion or tracheoplasty). If the FLS are in the trachea or mainstem bronchi, then a stent trial is performed (an algorithm to proceed directly with tracheoplasty has not yet been studied). If the FLS are not in the central airways, then stent insertion or tracheoplasty should not be offered, because they are unlikely to improve flow and alternative explanations for patient’s symptoms should be investigated. After stent insertion or tracheoplasty, a follow-up bronchoscopy or dynamic CT should be performed within 4 to 6 weeks to assess airway patency and potential adverse events. H&P, history and physical examination; +, improvement and –, lack of improvement after a specific intervention; dashed line, an alternative strategy, depending on availability/expertise with technique.
8 days (range, 4–92 days), of which 3 days (range, 0–91 days) were in the intensive care unit. Two patients (3.2%) died postoperatively and overall complications were seen in 38% of patients and included a new respiratory infection, pulmonary embolism, and atrial fibrillation. Six patients (10%) required reintubation and 9 (14%) received a postoperative tracheotomy, including 4 tracheotomies intraoperatively immediately after the tracheobronchoplasty in anticipation of the need for frequent therapeutic aspiration bronchoscopy and tracheal suctioning, which was needed in 47 of 66 patients. A less invasive approach used video-assisted thoracoscopic surgical tracheobronchoplasty combined with airway stent placement for the treatment of 2 cases of TBM.129 The anecdotal evidence and concurrent use of stents raise questions about the long-term benefits of the combined modality.

### Treatment strategies: key points

1. Asymptomatic ECAC, regardless of the degree of AC, should not be treated.
2. Treatment of the underlying cause must be attempted before considering more invasive interventions.
3. NIPPV-assisted bronchoscopy allows titration of applied pressures that maintain airway patency during expiration.
4. Intraluminal airway pressures measurements localize the choke points and may predict response to interventions.
5. Focal disease can be treated by resection or reconstruction or bypassed with an indwelling tracheostomy tube.
6. Significantly impaired patients with severe and diffuse EDAC or crescent TBM may benefit from membranous tracheoplasty.
7. Inoperable patients with refractory symptoms may benefit from silicone stent insertion.
8. Most patients with ECAC and indwelling airway stents require frequent bronchoscopic interventions to manage stent-related mucus obstruction, migration, and granulation tissue.

### SUMMARY

TBM is characterized as weakened or destroyed cartilage in the central airways, resulting in expiratory flow limitation. EDAC is characterized by excessive bulging of the posterior membrane inside the central airway lumen. ECAC is a syndrome that includes both TBM and EDAC. Depending on the degree of AC, anatomic site, and respiratory maneuver used for defining it, EDAC is seen in normal individuals, those with morbid obesity, and those with a variety of obstructive ventilatory disorders. A careful physiologic assessment of the impact of ECAC on airflow and functional status is warranted before treatment. Identification of the flow-limiting airway segments can be obtained by performing functional bronchoscopy before invasive interventions. Even when the central AC is identified as responsible for symptoms, we suggest a conservative approach with medical treatment and NIPPV before committing patients to potentially harmful effects resulting from airway stents or open surgical procedures.

### REFERENCES


70. Boiselle PM, O’Donnell CR, Loring SH, et al. Reproducibility of forced expiratory tracheal collapse:


