

Exertional Dyspnea and Excessive Dynamic Airway Collapse



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KEYWORDS

- Dyspnea • Exercise • Excessive dynamic airway collapse • Tracheobronchomalacia
- Asthma • Chronic obstructive pulmonary disease

KEY POINTS

- Excessive dynamic airway collapse (EDAC), which is functional large airway collapse, can occur during exercise.
- EDAC symptoms include exertional dyspnea and centralized expiratory wheezing.
- EDAC may be identified in patients with chronic obstructive pulmonary disease or asthma.

INTRODUCTION

Excessive dynamic airway collapse (EDAC) is a recent term applied to individuals identified with functional collapse of the large airways. It is generally defined as excessive bulging of the posterior tracheal membrane into the airway lumen (usually >75%) during expiration without cartilage collapse to distinguish this entity from tracheobronchomalacia (TBM).¹ It has been primarily associated with underlying airway disorders, such as chronic obstructive pulmonary disease (COPD), asthma, and bronchiectasis.² Those patients with moderate to severe symptoms can present with cough, wheezing, dyspnea, or recurrent respiratory infections related to exacerbations of their lung disease. Likewise, it may become symptomatic after mild to moderate exertion. Current guidelines suggest that functional status (exertion, daily activities, or rest), length of

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the tracheobronchial wall affected, and severity of collapse are also important to define in patients diagnosed with EDAC.²

Much of the description of EDAC has focused on exacerbations of underlying disease with little discussion on its relationship to exercise. Weinstein and colleagues³ recently published a case series of 6 individuals in the military with symptomatic EDAC only during exercise. All had exertional symptoms, expiratory wheezing, and confirmed visual evidence of large airway collapse (>75%) with fiberoptic bronchoscopy (FOB). The findings have expanded the differential in the challenging evaluation of exertional dyspnea patients with otherwise normal pulmonary function testing (PFT) and chest imaging.⁴ In this review, the authors aim to discuss the relationship between exercise and EDAC and further elucidate its potential impact on exercise limitation.

EXCESSIVE DYNAMIC AIRWAY COLLAPSE DEFINITION

EDAC is generally defined as excessive bulging of the posterior tracheal membrane during expiration with greater than 75% collapse of the airway lumen. It is distinctly different from TBM because of the absence of cartilaginous involvement. These distinct clinical entities may be very similar in presentation and have been referred to collectively as expiratory central airway collapse.² However, there is no universally accepted cutoff value to separate normal from abnormal expiratory airway narrowing, but generally greater than 75% closure of the airway lumen has been suggested to be clinically important.

Reflecting tidal cycling of intrathoracic pressure, there is inward bulging of the posterior membrane of the trachea and main bronchi that occurs normally during exhalation. This airway compression, known as dynamic airway collapse, can ordinarily narrow the lumen of normal central airways by up to 50%. Posterior membrane collapse has also been described to be partly physiologic and associated with forced expiration or cough. Defining the clinical significance of EDAC can be problematic as functional airway collapse in healthy individuals has been documented. There is a wide variation in bronchial collapse with forced expiration on multidetector computed tomographic (CT) imaging in healthy volunteers with normal PFT and no significant smoke exposure.^{5,6}

PATHOPHYSIOLOGY

It is currently theorized that large airway collapse related to EDAC is due to increased airway resistance distal to the equal pressure point, decreased lung elastic recoil, and increased pleural pressures. During exercise itself, there is increased luminal airflow velocity leading to a decrease in luminal pressures, especially in tapering airways, and creating a stress on luminal integrity with subsequent smooth muscle fatigue or strain. This muscle lassitude in the setting of continued pressure differential is the likely culprit for why this change in airway diameter is not identified on nonexertional pulmonary testing.⁷

The pathogenesis of EDAC has been described as being a result of 2 primary circumstances. One factor is weakening of the smooth muscle tone of the posterior membrane. The other factor is a decrease in luminal pressures in regions of tapering airways (Bernoulli's principle) in the setting of reduced elastic recoil, thus creating even greater narrowing leading to greater transmural pressure gradient.⁸ The diagnosis of EDAC has primarily been described in patients with underlying lung disorders such as COPD or asthma, especially in those patients with identifiable TBM. The underlying lung pathology likely contributes to the chronic atrophy and strain of

longitudinal smooth muscle given the excessive airway pressure gradients typically seen in these disease processes.⁹

EDAC as seen on FOB or dynamic chest CT imaging occurs at the compressible segment of the central airway proximal to the equal pressure point. Likewise, tracheal collapse is caused by increased airway resistance distal to the equal pressure point, decreased lung elastic recoil, and increased pleural pressure. This mechanism explains the finding of EDAC in patients with uncontrolled asthma, COPD, and obesity, especially when 2 or more of those disorders coexist.¹⁰ When EDAC is defined as a forced expiratory collapse of greater than 80% of the airway lumen, there is no significant correlation between end-expiratory or dynamic expiratory collapse and percent predicted forced expiratory volume at 1 second (FEV₁).⁷ Consistent with the hypothesis that EDAC is typically a consequence of peripheral airway disorders and not central airway pathology, there is documented improvement in EDAC after lung transplantation or lung volume reduction surgery in patients with emphysema. However, the mechanism in patients without underlying lung pathology as described by Weinstein and colleagues³ has not been elucidated.

EXCESSIVE DYNAMIC AIRWAY COLLAPSE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND ASTHMA

EDAC is most often associated with COPD. The largest study documenting the prevalence of EDAC in COPD described an overall prevalence of 6% in COPD patients.¹¹ Prior studies have demonstrated an EDAC prevalence from 9% to 22% in COPD.^{10,12–15} The definition used for EDAC varied across the studies, with a greater than 50% to 80% decrease in cross-sectional area (CSA) used. In addition, the methods used to identify EDAC were not uniform and included FOB, dynamic CT scan, and end-expiratory CT imaging. In COPD patients, EDAC is associated with a higher GOLD (Global Initiative for Chronic Obstructive Lung Disease) stage, increased airflow limitation on spirometry, worsened dyspnea scores, and increased frequency of severe COPD.¹¹ EDAC has also been implicated as a potential cause of persistent wheezing in COPD patients; up to 40% with persistent wheezing have been found to have EDAC.¹⁶

An increased body mass index (BMI) is also associated with an increased prevalence of EDAC in COPD. Two studies found a statistically significant association with BMI; both studies evaluated COPD patients and found that a higher BMI, greater than 30 and 35, were linked with the finding of EDAC.^{11,17} Furthermore, there was not an association with BMI and EDAC in those patients without COPD.¹⁷ Whether EDAC causes clinically important flow limitation remains a subject of current debate. In a recent study of patients with COPD, no significant correlation was observed between the degree of static end-expiratory or dynamic forced expiratory tracheal collapse and FEV₁ percent predicted.¹⁰ However, a secondary analysis of patients enrolled in the US National Institutes of Health COPD Gene study did reveal an adverse association between EDAC and quality of life as measured by the St George's Respiratory Questionnaire (SGRQ).¹¹

Most of the evidence linking asthma with EDAC is in the form of case reports of difficult-to-control asthma with subsequent identification of EDAC.^{18,19} One study has prospectively evaluated 202 asthmatic patients with FOB and identified a prevalence of 31%, noting that the EDAC prevalence increased with the severity of asthma.²⁰ There are no available data regarding the impact of EDAC on asthma exacerbations, quality-of-life scores, or exertional symptoms. In addition, it is unclear from the published data whether the cases presented truly have asthma or if EDAC is the primary underlying cause merely mimicking asthma.^{18,19}

EXCESSIVE DYNAMIC AIRWAY COLLAPSE AND FUNCTIONAL CAPACITY

The impact of EDAC itself on functional capacity is unknown because most of the data are derived from the COPD population. In the largest cohort of EDAC patients, it was demonstrated that EDAC leads to increased dyspnea and poorer respiratory quality of life, but there was no impact on 6-minute walk testing (6MWT).¹¹ In addition, a small series of both EDAC and TBM patients ($n = 18$) who underwent airway stenting identified that half had improvement in their modified World Health Organization (WHO) functional classification.²¹ In this study, patients with the more severe cases showed improvement, whereas the milder cases did not. Boisselle and colleagues¹² studied 100 COPD patients with full PFTs, 6MWT, SGRQ, and dynamic CT scanning. Twenty percent of the patients were identified with expiratory collapse based on greater than 80% expiratory reduction in the tracheal lumen CSA during the expiration phase of CT scanning. This study was unable to identify differences in FEV₁, diffusing capacity, 6MWT, or SGRQ activity scores between COPD patients without and with excessive tracheal collapse, respectively. Represas-Represas and colleagues¹⁵ studied 53 COPD patients with collapse at different levels by dynamic CT imaging and did not demonstrate differences in Medical Research Council dyspnea index scores or 6MWT.

EXERCISE-ASSOCIATED EXCESSIVE DYNAMIC AIRWAY COLLAPSE

Weinstein and colleagues³ published a unique case series of 6 patients identified during comprehensive evaluation for post-deployment respiratory symptoms. Most notably, this group of patients reported symptoms of audible “wheezing” with exertional dyspnea. None of the patients were found to have evidence of underlying obstructive or interstitial lung disease. High-resolution computed tomography (HRCT) was notable for significant expiratory collapse in 2 patients, whereas dynamic CT demonstrated collapse in an additional 2 patients. Four of the patients had audible expiratory large airway wheezing that developed during exercise (not present at rest) with further localization by chest auscultation, and the 2 remaining patients had expiratory wheezing localized only by auscultation. Flexible bronchoscopy was able to localize the site of obstruction (>75% obstruction of the affected airway) that corresponded directly to the auscultatory findings. This included 2 patients who underwent awake exercise FOB used to identify the site of obstruction (see video file from Weinstein and colleagues³). These 6 individuals were identified with exercise-associated EDAC using the following criteria:

1. Exertional dyspnea without resting symptoms,
2. Focal expiratory wheezing during exercise,
3. Functional collapse of the large airways during FOB,
4. Expiratory CT imaging with narrowing of the airway, and
5. Absence of underlying pulmonary pathology.³

EXCESSIVE DYNAMIC AIRWAY COLLAPSE EVALUATION

In most EDAC patients, typical symptoms may include chronic cough, dyspnea, wheezing, stridor, orthopnea, recurrent pulmonary infections, and impaired clearance of respiratory secretions. These symptoms may be triggered by numerous factors to include upper respiratory infections, dust exposure, exercise, recumbent positioning, forced exhalation, and cough.^{11,18,20,22,23} Immediate onset of dyspnea with exertion may differentiate EDAC from COPD and asthma, whereby symptom onset with exertion may be more gradual.¹⁹ An initial step in identifying EDAC in any given patient is

careful physical examination, which may identify and localize airway sounds that are directly emanating from the large airways. Localization of an expiratory wheeze (which may be heard in all lung fields) to the central airways should prompt a clinician to further investigate. In patients identified with exercise-associated EDAC, this finding on lung examination prompted further imaging studies. This included either HRCT with expiratory images or a dynamic CT in which the patient actively performs a forced expiratory maneuver. In individuals with exertional symptoms, performing some type of exercise study may cause EDAC and wheezing not present at rest. Another important step in eliminating other causes is performance of exercise laryngoscopy to rule out laryngeal disorders, such as inducible laryngeal obstruction.²⁴

AIRWAY IMAGING (DYNAMIC COMPUTED TOMOGRAPHY)

Airway imaging in EDAC may demonstrate a significant change in the luminal CRA of the airway in the inspiratory and expiratory phases as demonstrated in numerous studies.^{1,11,12,23,25,26} CT imaging during inspiratory and expiratory phases may demonstrate dynamic collapse of the trachea and main bronchi during the expiratory phase with posterior membrane bulging, in contrast to TBM, which is associated with anterolateral wall collapse.^{18,25,27} Dynamic CT is the preferred imaging modality over static imaging, because the latter may lessen the degree of airway collapse.² Dynamic CT may be equal to FOB in the diagnosis of EDAC, providing an important noninvasive method of diagnosis.^{1,8,28} Although CSA narrowing greater than 50% is typically used to define EDAC for research purposes, there are data that normal individuals may have a 35% decrease in CSA, and one study of healthy volunteers found 78% of participants exceeded greater than 50% decrease in CSA.^{5,6}

FUNCTIONAL BRONCHOSCOPY

Fiberoptic bronchoscopy should be performed in all patients suspected of having EDAC to identify the presence or absence of EDAC and determination of the site of obstruction.^{8,18,29,30} Suggested specific indications for functional bronchoscopy are shown in **Box 1**. If possible, sedation should be minimized to allow the patient to follow commands to better demonstrate airway abnormalities associated with the inspiratory and expiratory phases. Fiberoptic bronchoscopy in EDAC may demonstrate narrowing of the airway lumen with expiratory maneuvers and more commonly with cough.^{13,23} One study evaluating estimates of the degree of airway collapse during FOB found high interoperator and intraoperator reliability, supporting the use of FOB in the diagnosis of EDAC.⁹ The use of endobronchial ultrasound in EDAC may

Box 1

Indications for functional bronchoscopy

1. Audible wheezing caused by exercise
2. Wheezing that localizes to the large airways on clinical examination
3. Concern for tracheobronchomalacia
4. Evidence of large airway collapse identified by CT scanning
5. Recurrent COPD or asthma exacerbations
6. Persistent wheezing despite treatment
7. Unexplained dyspnea after noninvasive evaluation

demonstrate normal anterior cartilaginous structures and thin posterior membrane.²¹ Findings consistent with EDAC may be evident in 5% to 23% of patients undergoing FOB for undifferentiated respiratory symptoms, and common findings include chronic inflammation, lymphocytic predominance, and negative cultures.^{22,25} In selected individuals with symptoms at higher levels of exercise, awake FOB during exercise (typically cycle ergometry) with the onset of symptoms was shown to be diagnostic.³

TREATMENT OPTIONS

Currently, there are few treatment options available to those patients identified with EDAC. Therapy primarily should center on treating the underlying disease process (COPD, asthma, bronchiectasis) to limit the number and frequency of exacerbations. Each exacerbation with resultant increases in wheezing, cough, and airway secretions may intensify the sensation of dyspnea because of increases in airway collapse. Primary treatment modalities for both TBM and EDAC also include the use of noninvasive positive pressure ventilation (NIPPV) to prevent large airway collapse. NIPPV functions to open the large airways and decrease the work of breathing, aiding in drainage of respiratory secretions and possibly improving nocturnal wheezing; it does not improve dyspnea and cough.^{1,23} Seven to 10 cm of water pressure is typically sufficient to increase intraluminal pressure, lung volumes, and elastic recoil and may be titrated during functional FOB.^{2,7} It is likewise important to screen for obstructive sleep apnea in patients with EDAC who require NIPPV.⁸ Notably, there is an ongoing study currently being conducted to evaluate daytime use of continuous positive airway pressure (CPAP) in patients with tracheomalacia.³¹

The use of mechanical airway stenting and possible tracheobronchoplasty is reserved for selected individuals with EDAC with severe symptoms and a significant limitation in overall functional classification (class III or IV).^{1,10} As described in several studies of patients with severe TBM, improvement of respiratory symptoms, quality of life, and WHO functional class occurred after airway stenting and/or surgical intervention in selected candidates.^{9,32} Aggressive interventions for EDAC are generally preferred only for cases refractory to conservative management and NIPPV whereby the potential benefit of the invasive procedure outweighs the associated risk.⁷

For EDAC symptoms related specifically to exercise, treatment options are very limited. It is not recommended for these patients to undergo airway stenting or tracheobronchoplasty based on the impact of disease. The authors have recommended to their patients with exercise-associated EDAC to limit exertional activities (running, jogging, and so forth) to a less strenuous pace or distance where symptoms such as dyspnea and audible wheezing are minimized. In this group of patients, reduction in exercise has been adequate to control their symptoms. In addition, consideration should be given for CPAP use if symptomatic at rest or after exercise.³¹ It is not known whether continued exercise will worsen the extent or severity of EDAC in this group of patients. Notably, several of the active duty military patients had to leave the military given their limitations with aerobic activity.

SUMMARY

EDAC (with or without underlying lung disease) is very likely aggravated by exercise and may be symptom limiting in many individuals. Given the increases in minute ventilation during exercise, increased flows are likely to make airway collapse more pronounced. Careful evaluation should be undertaken to identify patients with EDAC and its contribution to airway symptoms during exercise. Use of dynamic CT imaging

or FOB should help to identify patients with underlying EDAC and potentially alter treatment plans. Future priorities for defining this entity are as follows:

1. To more fully describe the role of exertional EDAC in patients with asthma through use of exercise bronchoscopy and
2. Increase the utilization of dynamic CT imaging and functional bronchoscopy in suspected large airway collapse.

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