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REVIEW ARTICLE

New insights in excessive dynamic airway collapse (EDAC) and tracheobronchomalacia

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ABSTRACT

Excessive central airway collapse (ECAC) encompasses both excessive dynamic airway collapse (EDAC) and tracheobronchomalacia (TBM). This review aims to synthesize current knowledge of ECAC, including its pathophysiological mechanisms, clinical presentation, diagnosis and management strategies. It also addresses existing gaps and controversies in our current understanding. Lastly, it highlights recent insights into the understanding and management of ECAC, offering a comprehensive overview of the evolving landscape of this condition.

Keywords: Dynamic airway collapse. Tracheomalacia. Tracheobronchomalacia. Large airway collapse. Excessive central airway collapse. Bronchoscopy.

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INTRODUCTION

In medical literature, there has historically been a degree of ambiguity surrounding the differentiation between excessive dynamic airway collapse (EDAC) and tracheobronchomalacia (TBM), often leading to their interchangeable use. Despite their distinct pathological basis, both conditions manifest as an exaggerated collapse of the central airways during expiration, thereby falling under the overarching classification of excessive central airway collapse (ECAC)[1].

In this article, we will synthesize current understandings of EDAC and TBM, highlight existing gaps and controversies, review new insights and explore future perspectives aimed at advancing our understanding and management of these conditions.

Current understandings on excessive central airway collapse

During expiration, alveolar pressure propels gas from the alveoli towards the large airways. At the point at which intraluminal pressure equals extraluminal pressure (i.e. the equal pressure point or EPP) the airway becomes divided into two segments: upstream (towards distal airways) and downstream (towards proximal airways). Upstream, positive transpulmonary pressure helps maintain the distal airways open. Downstream, negative transpulmonary pressure facilitates the dynamic collapse of central airways, which aids in the clearance of bronchial secretions[2]. If the airflow in the central airways decreases, such as in patients with increased resistance in small airways or reduced elastic recoil pressures (e.g., obese individuals breathing at lower lung volumes), the dynamic collapse of the central airways might increase. An excessive collapse may disrupt airflow, increase turbulence within the airways, and potentially impede bronchial clearance[2].

In patients with TBM, the weakening of the tracheobronchial cartilage walls directly contributes to the excessive collapse of the airway. Although this weakening may be limited to isolated segments, it often progresses to diffuse involvement. During forced expiration in patients with TBM, the trachea may adopt various morphologies, including crescent or saber-sheath shapes depending on the affected walls (anterior or lateral, respectively), and a circumferential or concentric shape when both walls are weakened. On the other hand, in patients with EDAC, the "excessive" inward bulging of the posterior wall may be attributed to weakness and atrophy of the muscular fibers[1,3,4]. It is noteworthy, however, that the definitive classification of EDAC as a central airway pathology or its association with peripheral airway disorders remains unclear[5,6]. The etiologies of ECAC are listed in table 1.

The ECAC (or LAC, for large airway collapse) syndrome encompasses both EDAC and TBM. It is characterized by severe respiratory symptoms, including a distinctive barking, seal-like, or honking cough, along with compromised airway clearance leading to respiratory tract infections and exertional dyspnea. Although these symptoms often result in functional limitations and a diminished quality of life, their nonspecific nature, is frequently mistaken for asthma or chronic obstructive

Table 1. Etiology of Excessive Central Airway Collapse (ECAC)

Congenital
– Abnormalities of the cartilage (e.g. achondroplasia, chondromalacia) – Developmental anomalies of the respiratory tract (e.g. prematurity, bronchopulmonary dysplasia) – Associated to gastrointestinal anomalies (e.g. esophageal atresia, tracheo-esophageal fistula) – Syndromes associated with TM/TBM (e.g. Marfan's, Ehlers-Danlos) – Tracheobronchomegaly (Mounier-Kuhn)* – Idiopathic
Acquired
– Associated with chronic compression from anatomical anomalies/deformities (e.g. double aortic arch, severe pulmonary arterial hypertension, scoliosis, pectus excavatum) – Associated with severe or repeated infections (e.g. severe tracheobronchitis, bronchiectasis, cystic fibrosis) – Associated with inflammatory processes (e.g. relapsing polychondritis, radiation therapy, mustard gas exposure) – Associated with chronic extrinsic compression (e.g. goiter) – Associated with laryngeal, tracheal and bronchial surgery – Iatrogenic (e.g. prolonged intubation, tracheostomy) – Associated with peripheral airway obstruction (e.g. obesity, asthma, COPD) – Idiopathic

*Probably both congenital and acquired forms, unclear.
COPD: chronic obstructive pulmonary disease; TBM: tracheobronchomalacia; TM: tracheomalacia.
Adapted from Wallis et al.[7]

pulmonary disease (COPD), which can lead to misdiagnosis or delayed diagnosis[8]. This issue, compounded by confusing terminology and a lack of consensus on what degree of collapse constitutes "excessive" in the literature, likely contributes to the underestimation of ECAC prevalence. Reported data to date suggests ECAC may be present in 2-17% of healthy individuals and between 20-27% of patients with COPD or asthma[9].

Demonstrating the presence of ECAC is challenging since its symptoms frequently overlap with those of other more prevalent respiratory conditions, but the presence and severity of ECAC do not correlate with abnormalities in pulmonary function tests, respiratory symptoms or the degree of impairment in quality of life scales[10]. Therefore, in patients whose respiratory symptoms are not fully explained by other diagnoses (often coexisting) or in those with partial or no clinical improvement with appropriate treatments, it is recommended to rule out the presence of ECAC through dynamic airway computed tomography and/or dynamic flexible bronchoscopy, both performed under forced expiratory maneuvers.

Dynamic expiratory airway CT imaging emerges as a highly sensitive method for identifying airway malacia, demonstrating agreement with the gold standard dynamic flexible bronchoscopy[3,11]. When reporting the severity of the collapse, most recent studies use the following thresholds: < 70% normal, 70-80% mild, 81-90% moderate, > 90% severe[8,11]. While both imaging techniques prove valuable for delineating the morphology, severity, and distribution of the disease, it is worth noting that this generalization stems from a small cohort observed within a single, highly experienced center[12]. In fact, the vast majority of published studies on ECAC have relied on imaging modalities, particularly computerized tomography (CT) scans[9]. Therefore, it seems reasonable to utilize dynamic CT as a minimally invasive pre-test. However, in more severe cases where more invasive treatments need to be considered, a dynamic flexible bronchoscopy allows for a more thorough exploration of the airways' degree of collapse, morphology and microenvironment. To date, only three studies have investigated the use of dynamic flexible bronchoscopy in assessing airway collapse, despite it being considered the "gold standard" for diagnosing ECAC. In these studies, airway collapse was evaluated at different levels, including the trachea,

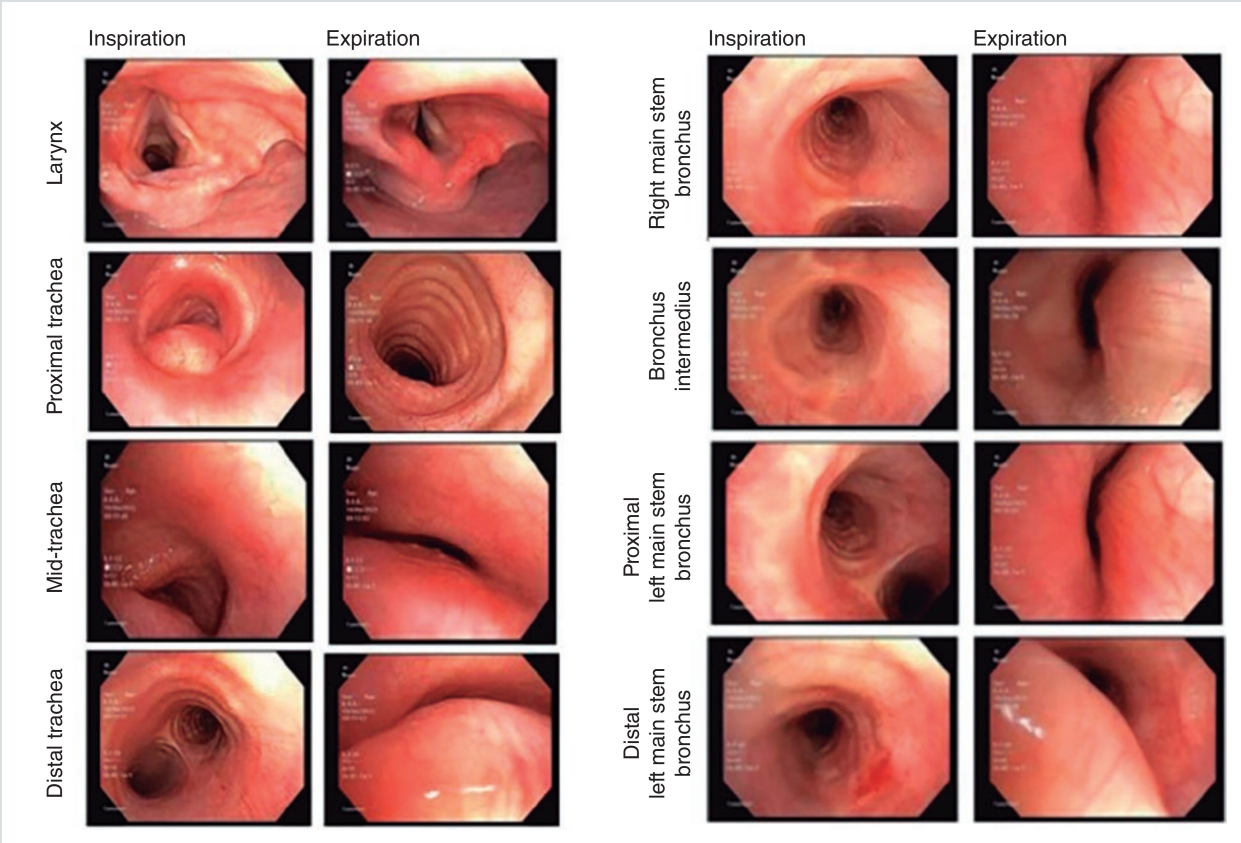

Figure 1. Dynamic flexible bronchoscopy. Several frames at various stages of the respiratory cycle are captured, using the difference between maximal and minimal diameters as a reference for visually estimating the degree of airway collapse.

carina, and main bronchi. Bronchoscopies were performed under light sedation and involved breathing maneuvers, including forced inspiration and expiration. Luminal dimensions were measured at different sites, providing semi-quantitative descriptions[13–15]. In figure 1, several frames of a dynamic bronchoscopy are shown.

Because dynamic flexible bronchoscopy is based on the visual assessment of the degree of collapse, previous work has been done to perform airway measurements. In one study, acetate grids (i.e. transparent plastic sheets with a square pattern) over video recordings were used to compare the difference in the numbers of squares enclosed in an airway segment at minimal and maximal surface area[16]. Another study assessed airway caliber in a dog after bronchoscopy image distortions were corrected[17]. Other researchers utilized manual tracings of the trachea to establish the relationship between maximal and minimal areas, referred to as the shape index (Fig. 2)[18].

The initial management of symptomatic ECAC involves investigating and treating frequently encountered concurrent conditions, such as obesity, peripheral airway obstruction, vocal

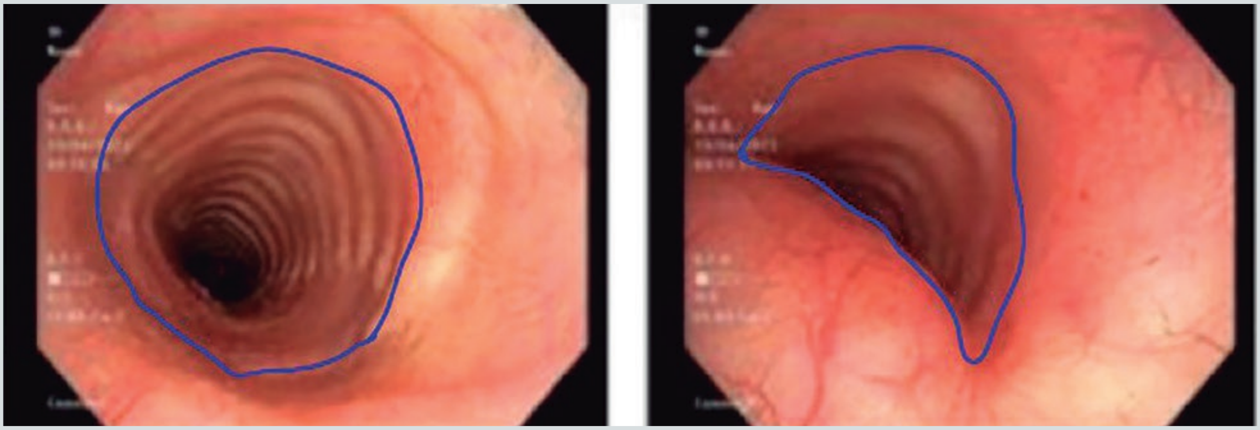

Figure 2. Measurement of degree of airway collapse. Tracheal cross-sections were manually traced at different stages of the respiratory cycle. The shape index was computed by dividing.

cord dysfunction, allergic cough and gastroesophageal reflux disease[19]. Additionally, comprehensive care for cough, respiratory infections, and dyspnea resulting from dynamic central airway collapse should involve pulmonary rehabilitation and physiotherapy, antimicrobial therapy, and perhaps some type of positive airway pressure support like pursed lip breathing, positive expiratory pressure (PEP) device (e.g. PEP Buddy[20] or Acapella®), continuous positive airway pressure (CPAP) or non-invasive ventilation (NIV)[8,19,20].

In cases of severe symptomatic ECAC (> 90% dynamic airway collapse) where medical management falls short, a short-term stent placement trial (7 to 14 days) with pre- and post-symptomatic and physiologic assessment is advised to evaluate potential symptom relief and identify candidates for surgical central airway stabilization. Stents are strategically placed in the trachea, main stem bronchi, and right bronchus intermedius to address severe malacia, with stent length tailored to the affected airway segment to minimize the impact on mucociliary clearance. Post-stent care is crucial to prevent complications and accurately assess symptom improvement. A recent study showed that uncovered self-expanding metallic stents had less mucus plugging compared with silicone y-stents (0% versus 38.5%) ($p > 0.04$) and provided a greater improvement in dyspnea, cough and exercise capacity. A successful stent trial is determined by symptomatic and/or objective improvement in respiratory symptoms, quality of life questionnaires, and/or lung function tests. Most importantly, a recent study showed that a positive stent trial predicts subsequent success of tracheobronchoplasty (TBP)[21]. Lack of improvement post-stenting may require more intensive medical treatment, while significant improvement may prompt consideration for definitive surgical intervention with TBP[22]. For patients ineligible for surgical intervention, intensified medical management should be pursued, with long-term stenting considered only in highly selected cases. Some experts advocate using 3-D-designed personalized stents to minimize stent-related complications[23,24].

Based on case series, other researchers have proposed the use of CPAP in patients with ECAC to mitigate airway collapse. Pressure needs should be tailored and assessed during CPAP-assisted bronchoscopy or, alternatively, during CPAP-assisted CT scanning[25,26]. Another option could be to prescribe CPAP for nighttime use, rehabilitation sessions, and during respiratory exacerbations. However, these practices are confined to isolated experiences without any supporting evidence to date.

TBP involves stabilizing the airway by suturing a polypropylene mesh to the posterior membrane of the trachea and bronchi (see Fig. 3), with adjustments made depending on the type of ECAC. This surgical intervention has shown significant improvements in respiratory-related quality of life, dyspnea indices, and exercise capacity at one, two and five years. Although it carries considerable postoperative morbidity, the risk of mortality is low in experienced centers[29,30].

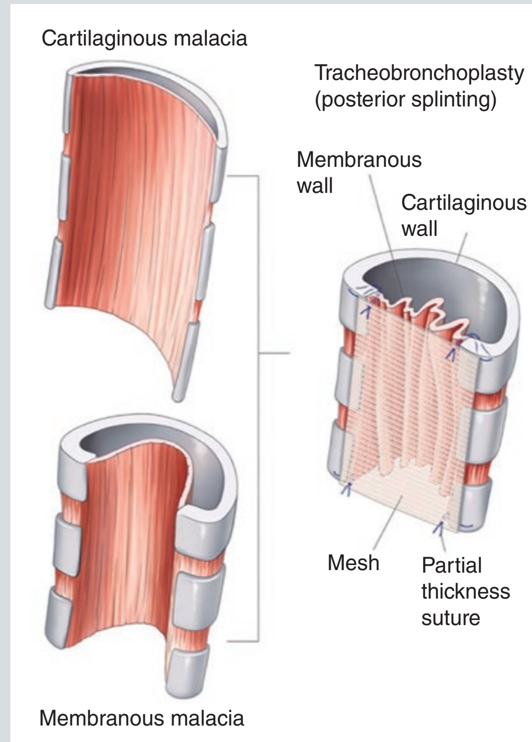

Figure 3. Tracheobronchoplasty. Posterior splinting with a mesh and sutures provide structural support and restore the shape of the airway, ensuring proper function and reducing airway collapse.

In all scenarios, attaining optimal outcomes relies on the collaborative efforts of a multidisciplinary airway team, operating in specialized centers with expertise to effectively evaluate and manage the unique challenges presented by this patient population[31].

Existing gaps and controversies in current understanding

One prominent concern in the current understanding of ECAC is the divergence in diagnostic criteria for defining a threshold for "excessive" collapse. This issue was highlighted in a systematic review spanning from 1989 to 2019, which identified 41 studies involving over 10,000 subjects. Notably, in half of these studies, the criterion for defining ECAC was a > 50% reduction in airway lumen or cross-sectional area (CSA), while in the remaining half, the cut-off threshold was higher (ranging somewhere between 70 and 80%) or directly left unspecified[9]. However, evidence from CT studies shows that this > 50% threshold is frequently exceeded by healthy individuals[3].

Related to this issue is the fact that dynamic bronchoscopy, considered the "gold standard" for evaluation of ECAC, relies on visual estimation for assessing the degree of airway collapse. However, contradictory evidence exists regarding the accuracy of visual estimation measures. While some studies have shown good correlation in the degree of collapse estimated by different observers[15], significant variability has been observed in visual estimation of the severity of collapse in other studies[32].

Nonetheless, aiming for standardization in endoscopic evaluation of ECAC is essential to enhance diagnostic precision, establish a clear and relevant threshold distinguishing between normal and excessive collapse, and determine what constitutes clinically relevant "excessive" collapse once accurate and reproducible measurements are obtained. Ultimately, this standardization is crucial not only for improving diagnostic accuracy but also for ensuring more effective treatment strategies for ECAC.

NEW INSIGHTS

Over the past five years, a significant volume of literature has emerged, contributing to our understanding of EDAC and TBM. While many of these publications delve into various aspects of these conditions, perhaps the most significant advancements have been witnessed in disease management. In the next paragraphs, we aim to highlight key findings and breakthroughs that have emerged from recent research endeavors, providing a comprehensive glimpse into the evolving landscape of ECAC.

A recent study by Singh et al.[33] investigated the histopathological characteristics of tracheal specimens from patients with TBM and tracheal stenosis. Through a comparison of surgical resection specimens, the researchers observed alterations in the quality and density of elastin fibers in the posterior membrane of patients with TBM. Additionally, significant changes in the expression of genes encoding immune mediators and tissue remodeling factors were noted within the tracheal walls of individuals with both TBM and tracheal stenosis compared to control subjects. Whether these changes are involved in TBM pathogenesis or are merely associated with disease progression remains to be investigated.

Concerning the standardization of diagnostic criteria, a more pragmatic approach has been proposed. That is, determining a numerical score for the grade of collapsibility at six different levels of the main airways and providing a single overall score per patient that is the sum of these scores. This study found that a score of nine effectively distinguishes between severe and non-severe ECAC, with a sensitivity of 94% and a specificity of 74%, which is useful to assess the need for stent evaluation and TBP[34].

Other significant advances have occurred in the field of treatment. In this regard, a significant issue that has previously lacked standardization is the use of physiotherapy as the pivotal treatment for improving symptoms and overall quality of life for individuals with ECAC. A recent publication addressing this field introduces a structured approach known as the ABC method. This evidence-based evaluation and intervention method encompasses airway clearance techniques aimed at augmenting ventilation and airway hydration (such as an active cycle of breathing, positive expiratory pressure, oscillatory devices, CPAP, NIV, and mucolytics), breathing exercises and pattern reeducation to reduce airflow turbulence and maintain airway patency, and exercise capacity enhancement through various techniques, including the use of CPAP during ambulation[2].

In the field of interventional treatments, the effects of electrocautery, radiofrequency ablation, potassium titanyl phosphate laser, and precise argon plasma coagulation (APC) were evaluated on the tracheobronchial tree of four sheep cadavers, and the histologic changes consistent with acute thermal injury were described. Treatment effects were observed with all techniques across tissue layers, with varying degrees of damage. However, APC consistently produced more pronounced thermal injury across all layers compared to other modalities, without complete erosion, thus preserving potentially viable tissue[35]. After evaluation in the ex vivo model, they evaluated the effect of bronchoscopic APC on the posterior membrane of adult live sheep. They reported no significant clinical events during the 30-day follow-up period, with no signs of complications on CT chest imaging or bronchoscopy. After euthanasia, histopathology and gene expression were evaluated. The treated areas showed adequate healing with complete reconstitution of the epithelium, and an increase in fibroelastic collagen deposition was observed. APC treatment also upregulated the expression of fibrosis-associated genes. These findings suggest that APC may be a promising option for patients with severe symptomatic EDAC who are not candidates for surgical intervention[36].

Emerging advancements in the endoscopic management of ECAC include the development of helical nitinol stents, which have demonstrated potential for offering radial support while addressing mucus clearance limitations and providing atraumatic removal[37], as well as the use of personalized 3D-printed bioresorbable splints[38]. Finally, another interesting work has been the development of an ex vivo trachea model capable of producing mild, moderate, and severe tracheobronchomalacia for testing airway stents and optimizing new designs[39].

Regarding the type of stents used in stent trials prior to TBP, a retrospective review of 42 consecutive patients comparing uncovered self-expanding metallic airway stents (USEMAS) and silicone Y-stents (SYSs) demonstrated that the use of USEMAS led to a lower complication rate, a greater improvement in health-related quality of life and exercise capacity, and appeared to better predict how the patients would respond to TBP compared to SYSs[40]. It is worth noting that a newer approach has been proposed to evaluate surgical candidacy based on applying CPAP during exercise (pneumatic stenting) in a patient with cough-predominant ECAC[41]. Although it may be useful in this scenario, some experts believe that the use of PAP as an alternative to a stent trial in patients with dyspnea may overestimate the benefits of central airway stabilization and recommend not being used routinely until additional evidence is available.

To assess whether improvement during stent evaluation was sustained after TBP, a retrospective analysis was conducted on 120 patients who underwent stent evaluation followed by surgical stabilization. The results revealed the substantial enhancements in cough-related quality of life, modified Medical Research Council (mMRC) scores, and performance on the six-minute walk test (6MWT)

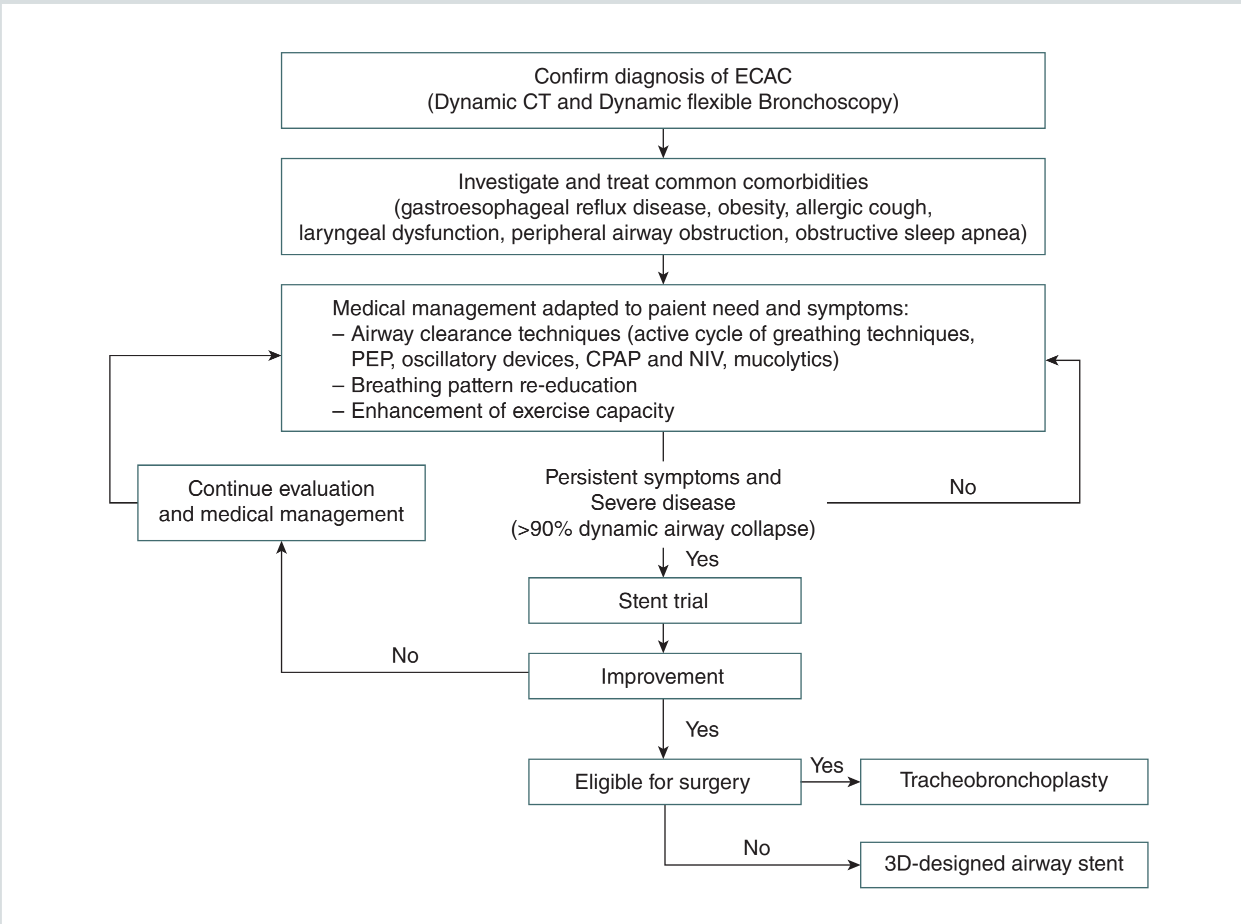

FIGURE 4. Management of Excessive Central Airway Collapse (ECAC).
CPAP: continuous positive airway pressure; NIV: non-invasive ventilation; PEP: positive expiratory pressure.

were sustained even after one year post-TBP, underscoring the enduring advantages of this surgical intervention[21]. Moreover, another study examined the long-term anatomic and clinical effects of TBP in 61 patients with complete radiological follow-up up to five years post-TBP. The authors reported a significant reduction in the percentage of expiratory airway collapse, which remained durable over five years. Additionally, significant improvements were observed in quality-of-life measures as well as in functional status[42]. These findings underscore the increasing support for the effectiveness and sustained benefits of TBP in patients with severe central airway collapse.

Similar to other approaches, the transition from open thoracotomy to robotic-assisted thoracoscopic surgery (RATS) offers a minimally invasive approach with similar results and a significant decrease in the hospital length of stay. In the initial published series involving 42 patients who underwent RATS TBP, early and intermediate follow-up demonstrated notable enhancements in pulmonary function testing and substantial patient satisfaction when compared to preoperative measurements, with a low risk of morbidity and mortality[43,44].

A recently introduced method known as laser TBP, yielded promising results in a cohort of ten patients diagnosed with membranous TBM, offering a potential alternative to both stenting and open TBP[45]. This approach needs to be further studied before being considered for routine use.

Finally, another publication has highlighted the importance of the ECAC coordinator as a pivotal figure in the management of ECAC. This underscores the critical role of coordination in optimizing patient care. By streamlining communication and collaboration among multidisciplinary teams, the presence of an ECAC coordinator ensures a cohesive and comprehensive approach to patient management from initial assessment through treatment and follow-up. Integrating this approach into clinical practice holds promise for enhancing patient outcomes and improving the overall quality of care for individuals with ECAC[31].

In figure 4, an approach to management incorporating the latest advancements and future prospects is presented.

CONCLUSIONS

As evidenced by the discussion presented herein, it is evident that there is still a need for standardizing and familiarizing the respiratory community with the terminology, refining the diagnosis and determining what is considered "excessive" collapse in patients with ECAC. Throughout recent publications, significant advancements in the management of these conditions have taken precedence, reflecting the ongoing efforts to enhance patient care and outcomes.

Perhaps considering ECAC as a treatable trait, rather than focusing solely on distinguishing between different entities, could lead to more personalized management, improving patient outcomes and treatment strategies.

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