CHEST

COPD-Associated Expiratory Central Airway Collapse

Current Concepts and New Perspectives

Pengcheng Zhou, MD; Wei Yu, MM; Wensheng Zhang, MM; Jianli Ma, MM; Qianming Xia, MD; and Chengshi He, MM

TOPIC IMPORTANCE: COPD-associated expiratory central airway collapse (ECAC) is a frequently overlooked benign airway obstructive disease with complex causes and unclear pathologic and physiologic mechanisms. Although interventions such as noninvasive positive pressure ventilation, airway stenting, and tracheobronchoplasty have shown definite efficacy in the treatment of COPD-associated ECAC, the diagnosis and treatment of this disease remain challenging. This review provides a systematic evaluation and outlook on the epidemiologic features, causes, pathophysiologic characteristics, clinical manifestations, diagnosis, and treatment of COPD-associated ECAC.

REVIEW FINDINGS: COPD-associated ECAC is a benign airway narrowing disease with atypical clinical symptoms and unknown incidence and pathogenesis. Bronchoscopy is considered the gold standard technique for diagnosis of COPD-associated ECAC, with dynamic biphasic CT imaging as an alternative noninvasive method. Noninvasive ventilation treatment can be continued on a long-term basis. Temporary airway stents can alleviate acute and severe tracheobronchomalacia. Long-term stent implantation can be considered after a risk to benefit assessment. Although tracheobronchoplasty has a definite therapeutic effect in patients with severe tracheobronchomalacia, perioperative complications remain a serious issue, and long-term efficacy observation is required. Traditional chinese medicine, other positive expiratory pressure therapies, and lung transplantation have shown potential with limited evidence.

SUMMARY: Although COPD-associated ECAC is attracting considerable attention, its pathophysiologic mechanisms, diagnosis, and management are full of challenges. In the future, randomized controlled trials on different therapies using patient-centered outcomes, cost-effective analysis on different interventions, and consensus guidelines on COPD-associated ECAC will be urgently needed.

CHEST 2025; 167(4):1024-1043

KEY WORDS: COPD; current concepts; excessive dynamic airway collapse; new perspectives; tracheobronchomalacia

ABBREVIATIONS: ECAC = expiratory central airway collapse; EDAC = excessive dynamic airway collapse; PAP = positive airway pressure; QoL = quality of life; RCT = randomized controlled trial; R-TBP = robot-assisted tracheobronchoplasty

AFFILIATIONS: From the Department of Respiratory Medicine (P. Z., W. Y., W. Z., and C. H.), Hospital of Chengdu University of Traditional Chinese Medicine, the Clinical Medical School (P. Z., W. Y., and J. M.), Chengdu University of Traditional Chinese Medicine, the Department of Respiratory Medicine (Q. X), Dujiangyan Shoujia Hospital, Chengdu; the Department of Respiratory Medicine (W. Z.), Lezhi Hospital Affiliated to Hospital of Chengdu University of Traditional Chinese Medicine, Ziyang, and the Department of Respiratory Medicine (P. Z.), Xiaojin County People's Hospital, Dezhou, China.

Drs Zhou, Yu, and Zhang contributed equally to this manuscript and share the first authorship.

Drs Xia and He contributed equally to this work and shared the co-corresponding authorship.

CORRESPONDENCE TO: Chengshi He, MM; email: hcs6512@126.com

DOI: https://doi.org/10.1016/j.chest.2024.11.015

Expiratory central airway collapse (ECAC) is a frequently overlooked benign obstructive airway disease mainly including tracheobronchomalacia and excessive dynamic airway collapse (EDAC), which have similar clinical manifestations, but different pathologic processes.[1] Tracheobronchomalacia results from chronic inflammation and airway pressure changes, which lead to chondrocyte degeneration and necrosis and loss of airway wall support. In contrast, EDAC results from decreased tension in the trachea or bronchial membrane, which excessively protrudes into the lumen during expiration, causing airway stenosis. ECAC is diagnosed by bronchoscopy or biphasic chest CT imaging when the airway lumen is patent in the inspiratory phase and collapsed or occluded during expiration or coughing, thus exhibiting dynamic narrowing with respiration.[2] The cause of ECAC is complex, with COPD considered to be one of the most common causes of ECAC in adults.[3] Previous studies have shown that tracheobronchomalacia is detected in 50% to 69% of patients with COPD.[2,4] However, epidemiologic studies on ECAC in patients with COPD are lacking, and it has been suggested that misdiagnosis and missed diagnosis may be an issue.

COPD is a common chronic airway disease and a global public health issue.[5] COPD involves the destruction of the small airways structure and formation of pulmonary bullae without gas exchange function. In patients with COPD, ECAC contributes independently to exertional dyspnea, reduced quality of life (QoL), and increased respiratory exacerbations.[6] The repeated airway narrowing observed in COPD-associated ECAC leads to ventilation dysfunction and poor secretion drainage, accelerates the deterioration of lung function, causes episodic choking, and even leads to syncope correlated with forced exhalation or cough.[7]

Although previous studies have shown the effectiveness of noninvasive mechanical ventilation, intra-airway stent implantation, and surgery for the treatment of COPD-associated ECAC, these procedures are associated with certain inherent limitations and complications, and effective therapeutic drugs are lacking.[8-10] This review summarizes the progress in the diagnosis and treatment of COPD-associated ECAC, providing a basis for future research.

Literature Search

A systematic search was conducted in PubMed, Cochrane Library, Web of Science, Google Scholar, China National Knowledge Infrastructure (China), and Embase using a controlled vocabulary and key words. Date and language restrictions were not applied. The last search update was performed on May 30, 2024. The Boolean search strategy was as follows: ((*tracheobronchomalacia* OR *tracheomalacia* OR *bronchomalacia* OR *expiratory central airway collapse* OR *excessive dynamic airway collapse*) AND (*COPD* OR *Chronic obstructive pulmonary disease* OR *emphysema*) NOT (*children* OR *infant*)). The studies were selected based on the following criteria: (1) definitive diagnosis and (2) relatively complete data (including information on patient demographics, history, bronchoscopy, imaging, treatment, and so on). The exclusion criteria include repeated reports of cases.

Evidence Review

Cause and Pathophysiologic Characteristics

COPD and ECAC have different anatomic distributions. COPD mainly involves the small airways. ECAC mainly occurs in the central airways, including the trachea, left and right main bronchi, and the bronchus in the middle segment of the right lung.[1] Tracheobronchomalacia in children usually is congenital,[11] whereas in adults it typically occurs secondary to tracheal intubation or incision, tracheal trauma, airway TB, COPD, bronchial asthma, thyroid tumors, gastroesophageal reflux disease, recurrent polychondritis, or mediastinal tumors (Table 1).[1,12] EDAC is relatively rare in children, whereas in adults it typically is associated closely with chronic obstructive airway diseases, such as COPD. Patients with COPD may experience tracheobronchomalacia or EDAC. A cohort study illustrated a strong association between tracheobronchomalacia and COPD, and this association was maintained roughly in each stage of COPD severity.[13] Another large cohort study also showed that the prevalence of ECAC was higher in patients with COPD than in those without COPD and increased with Global Initiative for Chronic Obstructive Lung Disease stage.[6] More than 50% of patients with ECAC have COPD.[6]

The pathogenesis of COPD-associated ECAC is unclear, but it is currently believed that tracheobronchomalacia is related to factors such as chronic airway inflammation, chronic tissue hypoxia, and repeated changes in airway pressure, leading to chondrocyte and matrix degeneration (Fig 1), whereas EDAC is caused by the reduction of longitudinal elastic fibers of the airway membrane, leading to excessive relaxation of the

TABLE 1] Cause of ECAC

Airway inflammation
Inhalant of irritating substances
Chemical irritant inhalation (eg, cigarette smoke, fossil fuels, air pollution)
Aspiration or gastroesophageal reflux disease
Chronic airway infections (eg, cystic fibrosis, primary ciliary dyskinesia, bronchiectasis, immunodeficiency disease, and so on)
Common lung diseases (eg, COPD, asthma, and so on)
Collagen vascular disease (eg, recurrent polychondritis)
Prolonged intubation
Tracheotomy
Mechanical reasons
Damage or manipulation of the airway
Thoracic trauma
Tracheal surgery (lung resection, lung transplantation)
Tracheotomy
Postpneumonectomy syndrome
Intratracheal or endobronchial electrosurgery or laser treatment
After thyroid surgery
Chronic extratracheal compression
Extrathoracic malignancies: (carcinoma, teratoma, lymphoma, neuroblastoma of lung, thyroid, or esophageal, and so on)
Nonmalignant chest abnormalities: mediastinal goiter, vascular anomalies (aortic or pulmonary aneurysm, innominate artery, aortic arch ring, pulmonary artery sling, aberrant right subclavian), cysts (thymic cyst, bronchogenic cyst, lymphatic malformation), cardiac anomalies (enlarged left atrium, enlarged pulmonary arteries or veins), abscess, obesity
Congenital disease
Mounier-Kuhn syndrome
Hunter syndrome
Ehlers-Danlos syndrome

ECAC = expiratory central airway collapse.

membrane and protrusion into the lumen. A study showed that inhalation of corticosteroids by patients with COPD increased the risk of tracheobronchomalacia by 3.5 and 2.9 times compared with no inhalation and inhalation of low-dose corticosteroids, respectively.[14] Husta et al[15] suggested that EDAC and tracheobronchomalacia may be associated with an overdependence on inhaled corticosteroids. It remains to be determined whether ECAC is a specific physiologic

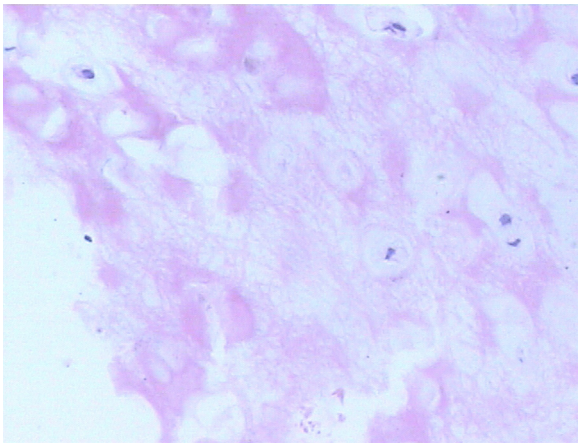

Figure 1 – *Photomicrograph showing histopathologic manifestations of tracheobronchomalacia: local dissolution and necrosis of tracheal chondrocytes, with slight infiltration of inflammatory cells (hematoxylin-eosin, original magnification ×100).*

phenomenon in patients with COPD or a complication of glucocorticoid therapy.[16]

The pathophysiologic mechanisms underlying COPD-associated ECAC can be elucidated by the relationship between intraluminal pressure of airway and pleural pressure (Fig 2). Physiologically, at the end of the inhalation phase, the pressure inside the lumen is greater than the pleural pressure by approximately 20 to 30 cm H_2O, and this difference causes the trachea to dilate.[17] At the end of exhalation, the intraluminal pressure inside the airway is almost equal to the pleural pressure, and the trachea is unstressed.[17] In COPD-associated ECAC, the airway support decreases owing to cartilage degeneration or insufficient membrane tension, and high transmural pressure can cause central airway collapse.

Epidemiologic Characteristics

A lack of consensus on the diagnosis of ECAC makes it difficult to establish its incidence, which has been reported to range from 4.5% to 44%.[18] In recent years, the detection of COPD in combination with tracheobronchomalacia or EDAC has increased (Table 2),[2,4,6,13,19-24] attracting considerable attention, and in 2023 the Global Initiative for Chronic Obstructive Lung Disease guidelines were revised to include the management of tracheobronchomalacia in patients with COPD.[25] Despite the growing number of studies indicating the importance of ECAC, poor awareness of this condition remains an issue.[26] In the future, physicians, especially respiratory physicians and radiologists, require further education on ECAC to

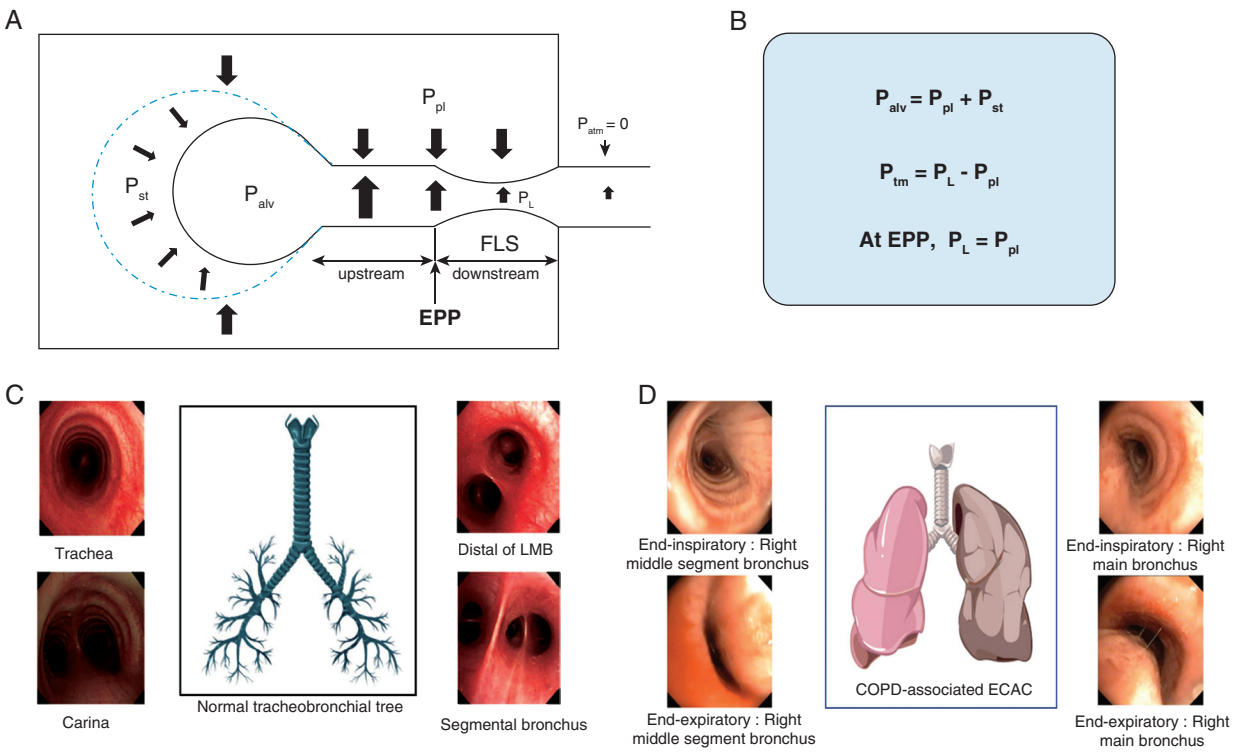

Figure 2 – *The pathophysiologic mechanisms underlying COPD-associated ECAC. A-B, Diagrams showing that P_{alv} causes air to flow during expiration and is approximately equal to P_{st} plus P_{pl}: $P_{alv} = P_{pl} + P_{st}$. During forced expiration, P_L becomes equal to P_{pl} at a point called EPP. EPP divides the airways into upstream segments, at which P_{tm} ($P_{tm} = P_L - P_{pl}$) is positive, and downstream segments at which P_{tm} is negative within the intrathoracic airways and positive within the extrathoracic airways. C, During normal expiration, increased intrathoracic pressure causes narrowing of the intrathoracic airway, which is counteracted by tracheobronchial rigidity, increased intraluminal pressure, and structural attachments. D, In COPD-associated ECAC, the airway support decreases owing to cartilage degeneration or insufficient membrane tension, and high P_{tm} can cause central airway collapse. ECAC = expiratory central airway collapse; EPP = equal pressure point; FLS = flow-limiting segment; LMB = left main bronchus; P_{alv} = alveolar pressure; P_L = intraluminal pressure; P_{pl} = pleural pressure of the lungs; P_{st} = recoil pressure of the lungs; P_{tm} = transmural pressure.*

enhance their understanding and management of the disease.

Clinical Manifestations

Most patients with COPD-associated ECAC have a history of long-term high-dose glucocorticoid inhalation, with nonspecific clinical manifestations that often overlap with those of COPD. The most common symptoms include wheezing, a bark-like cough, occasional asphyxia, forced expiration or cough-associated syncope, and dysfunctional secretion clearance, which can lead to sputum retention and recurrent pulmonary infections such as bronchitis and pneumonia.[7] Symptoms often worsen after exercise,[27] the Valsalva maneuver, postural changes (especially lying down), and forced exhalation or coughing, which can even cause death as a result of suffocation. Symptoms can worsen progressively, and many patients are misdiagnosed with refractory COPD.[3] A study conducted by our team but not yet published that included 88 cases of COPD-associated ECAC suggests that patients with COPD and ECAC excrete less sputum in the morning than those without ECAC, because it is difficult to expel phlegm when the central airway is collapsed more strongly during cough. The collapse of the extrathoracic trachea causes changes in breathing sounds during inhalation. Because the main lesions of COPD-associated ECAC are located in the chest cavity, changes in respiratory sounds during the expiratory phase often are heard.

Diagnosis

Currently, the diagnosis of COPD-associated ECAC requires the diagnostic criteria for COPD and ECAC to be met and other potential underlying diseases that may cause ECAC, such as tracheal intubation, tracheal TB, and recurrent polychondritis, to be excluded. Diagnosis of ECAC is made primarily based on the results of lung function tests, imaging, and bronchoscopy. The currently widely accepted standard is that when the cross-sectional area of the expiratory airway decreases by $>$ 50% compared with inhalation, ECAC needs to be

TABLE 2] Detection Rate of COPD-Associated ECAC

Reference	Patient Selection	No. of Participants	Trial Design	Diagnostic Method	Diagnostic Criteria	Outcomes
Inoue et al (2009)[19]	Pulmonary emphysema	56 (55 men, 1 woman; mean age, 68.9 y)	Retrospective analysis	Paired inspiratory-expiratory CT scanning with a low-dose technique (40 mA)	> 50% expiratory reduction in CSA at the end-expiratory phase	4 patients (7.1%) received a diagnosis of TBM
Ernst et al (2011)[2]	COPD comorbidities: GERD, 32%; OSA, 25%; asthma, 13%; intubation, 18%	238 (47% women and 53% men; median age, 65 y)	Retrospective analysis	Combination of airway CT imaging and dynamic bronchoscopy	> 50% expiratory reduction in CSA at the end-expiratory phase	103 patients (43%) received a diagnosis of COPD and moderately severe to severe TBM
Heussel et al (2004)[4]	COPD and healthy people who had never smoked	23 patients with COPD (median age, 59 y) and 15 volunteers (median age, 62 y)	Prospective study	Cine-MRI during continuous respiration	> 50% expiratory reduction in CSA at the end-expiratory phase	16 patients with COPD (69%) and 5 volunteers (33%) received a diagnosis of TM
Loring et al (2007)[20]	TBM comorbidities: COPD, 40%; GERD, 30%; OSA, 16%; asthma, 24%; bronchiectasis, 9%	80 (34 men, 46 women; mean [SD] age, 63 [12] y)	Prospective study	Bronchoscopy	> 50% expiratory reduction in CSA at the end-expiratory phase	32 patients with COPD (40%) received a diagnosis of TBM
Sverzellati et al (2009)[13]	COPD	71 (56 men, 15 women; mean age, 68.5 y)	Retrospective analysis	Inspiratory-dynamic expiratory MDCT imaging	> 50% expiratory reduction in CSA at the end-expiratory phase	38 (53%) patients with COPD have airway malacia; TBM was present in 18 patients (48%), BM was present in 13 patients (34%), and TM was present in 7 patients (18%)
Lee et al (2007)[21]	TBM comorbidities: COPD, 11; RP, 6; prior tracheostomy, 4; prior lung resection, radiation therapy, or both, 2	29 (12 men, 17 women; mean age, 60 ye)	Retrospective analysis	Combination of dynamic expiratory CT imaging and bronchoscopy	> 50% expiratory reduction in CSA at the end-expiratory phase	11 patients with COPD (38%) received a diagnosis of TBM

(Continued)

TABLE 2] *(Continued)*

Reference	Patient Selection	No. of Participants	Trial Design	Diagnostic Method	Diagnostic Criteria	Outcomes
O'Donnell et al (2014)[22]	COPD	67 (38 men, 29 women; mean age, 65.1 ye)	Prospective study	64-detector-row CT imaging at end-inspiration, during forced expiration, and at end expiration	None	Average forced expiratory collapse (62 ± 16%) was substantially greater than end-expiratory collapse (17 ± 18%)
Sindhwani et al (2016)[23]	COPD or asthma	25 (14 men, 11 women; mean [SD] age, 62.7 [7.81] y)	Pilot study	Combination of dynamic expiratory CT imaging and bronchoscopy	> 50% expiratory reduction in CSA at the forced expiration phase	10 patients with COPD or asthma (40%) received a diagnosis of TBM or EDAC
Represas-Represas et al (2015)[24]	COPD	53 (46 men, 7 women; mean age, 65 y)	Prospective study	Low-dose dynamic CT imaging	> 50% expiratory reduction in CSA at the end-expiratory phase	The percentage of collapse at each anatomic level of EDAC: aortic arch, 16.1%; carina, 19.4%; and bronchus intermedius, 21.7%
Bhatt et al (2016)[6]	Participants with and without COPD	8,820 patients (4,667 men, 4,153 woman; mean age, 59.7 y)	Prospective study	Paired inspiratory-expiratory CT scanning	> 50% expiratory reduction in CSA at the end-expiratory phase	443 patients with ECAC were identified; the prevalence of ECAC was higher in patients with COPD than in participants without COPD (5.9% [229/3,856] vs 4.3% [205/4,964]; $P = .001$)

BM = bronchomalacia; CSA = cross-sectional area; ECAC = expiratory central airway collapse; EDAC = excessive dynamic airway collapse; GERD = gastroesophageal reflux disorder; MDCT = multidetector CT; RP = relapsing polychondritis; TBM = tracheobronchomalacia; TM = tracheomalacia.

considered. Although previous studies have proposed different diagnostic thresholds and grading systems for ECAC (Table 3),[28-39] they all have different shortcomings, such as the inability to exclude some healthy individuals whose anatomic sites are more suitable for determining airway collapse and whose exhalation movements are more helpful for diagnosing ECAC. In the future, a multicenter study needs to determine which cutoff values, anatomic locations, and exhalation maneuvers have the greatest sensitivity and specificity for diagnosing ECAC.

Bronchoscopy: Currently, bronchoscopy is the gold standard for ECAC diagnosis.[27] Flexible bronchoscopy is preferred, because patients are able to breathe autonomously and follow instructions, allowing the observation of dynamic changes in the trachea and bronchi. Diverse movements, such as deep breathing, forced exhalation, coughing, and the Valsalva maneuver, have been suggested to enhance exhalation collapse. Although these maneuvers may increase the degree of airway collapse by increasing pleural pressure, they may not achieve the expected effect without special training on conducting these maneuvers before bronchoscopy. Currently, their diagnostic efficacy has not been validated. Therefore, it is necessary to conduct a comparative study of these maneuvers to determine whether they can help doctors diagnose ECAC. The main manifestations of ECAC observed using bronchoscopy are crescent, Saber-sheath-like, circumferential, or mixed morphologic changes (Figs 3, 4).[27] High-frequency endobronchial ultrasound using a 20-MHz radial scanning probe can identify low-echogenicity and high-echogenicity layers associated with the central airway laminar tissue structure; however, studies on its use in COPD-associated ECAC are lacking. Although bronchoscopy plays an important role in the diagnosis of ECAC, its inherent invasiveness has led researchers to explore other options.

Lung Function: Pulmonary function testing is the basis for the diagnosis and evaluation of obstructive airway disease; however, it has only a limited role in the diagnosis of ECAC. Although some studies have identified "inflection point," "biphasic morphology," "notch,"[40,41] and "flow oscillations"[42] in the expiratory branch of the flow-volume loop as characteristic of ECAC (Fig 5), other diseases such as OSA, laryngeal diseases, and neuromuscular diseases also exhibit this anomaly. Lung function test results therefore can provide evidence to support the diagnosis of ECAC, but cannot be the sole basis of this diagnosis. The decrease in lung function often is inconsistent with the severity of ECAC.[43] Majid et al[44] found that approximately 17% of patients with moderate to severe tracheobronchomalacia showed normal lung function and that most patients showed only a low forced peak expiratory flow rate. A study conducted by Loring et al[20] also showed that although patients with tracheobronchomalacia with flow limitation at rest showed greater tracheal narrowing than those without, the severity of expiratory flow limitation as measured by FEV_1 was not closely related to tracheal collapsibility.

Imaging: Biphasic dynamic chest CT imaging can be used to determine the extent of ECAC lesions in the airway lumen, to quantify narrowing, to observe airway morphologic features, and to evaluate distal bronchial lesions. The procedure is simple, relatively safe, and highly consistent with bronchoscopy, with an accuracy reported as 89% to 97% that of bronchoscopy (Fig 6).[45] Therefore, it represents a good alternative to bronchoscopy. Some studies have suggested that CT imaging should be performed at the end of inhalation, end of exhalation, and during exhalation.[21,46,47] Ciet et al[48] evaluated the role of cine MRI in the diagnosis of tracheobronchomalacia and found it to be a technically feasible alternative to multidetector CT imaging and bronchoscopy that avoids radiation exposure and anesthesia. Technetium-99m ventilation-perfusion single-photon emission CT imaging identified hypoperfusion in the left lung without ventilation in an 81-year-old woman with a suspected pulmonary embolism, which was diagnosed as tracheobronchomalacia after chest CT imaging and bronchoscopy.[49] Although single-photon emission CT imaging can help to detect airway stenosis through ventilation and perfusion scans, it cannot determine whether this narrowing is fixed or dynamic. In the future, further study is required to verify this approach.

Treatment

The priority in the treatment of COPD-associated ECAC is the management of COPD by the long-term and regular use of antiinflammatory and bronchodilator drugs and the addition of antibiotics and expectorants when an infection is present. ECAC then can be treated, with different methods adopted for different symptoms and severity. Currently, the treatment of ECAC in adults mainly involves noninvasive ventilation, airway stent implantation, and surgical procedures. Although other new therapies have proven effective in some case reports, these interventions come with low-level evidence and large-scale and multicenter trials are

TABLE 3] Different Cutoff Values or Classification Systems Used for ECAC

Reference	Cut Off Value to Define ECAC During Expiration	Comments
Rayl (1965)[28]	• > 50% airway narrowing during coughing • Extent: proximal (type I), mediastinal (type II), and intrapulmonary (type III) airways	Tracheobronchial collapse was assessed during cough on cinebronchography
Johnson et al (1973)[30]	Severity: 1° (50%-75% stenosis), 2° (75%-100% stenosis), 3° (100% stenosis), 4° (100% stenosis during coughing and airway dilation at rest) and focal	TM: > 50% collapse during coughing on fluoroscopy
Jokinen et al (1977)[29]	• Severity: mild (< 50%), moderate (50%-75%), severe (100%) • Extent: TM, TBM, BM	• TBM: expiratory reduction of ≥ 50% in the anteroposterior diameter of the airways • First classification based on bronchoscopic findings
Nuutinen (1977)[35]	> 50% expiratory reduction in sagittal diameter	• For tracheal and bronchial collapse • Used bronchoscopic estimations
Mair and Parsons (1992)[31]	• Severity: mild (< 70%), moderate (70%-90%), and severe (> 90%) • Cause: congenital (type 1), extrinsic compression (type 2), acquired (type 3)	• Described for pediatric TBM • Empirical severity score
Stern et al (1993)[36]	35% expiratory reduction in CSA in healthy individuals	• Only for tracheal collapse • Used paired inspiratory-dynamic expiratory CT imaging
Masaoka et al (1996)[39]	• > 80% expiratory narrowing • Cause and extent criteria • Pediatric, adult, and secondary	• For tracheal and bronchial collapse • Used bronchoscopic estimations and frontal and lateral radiographs to estimate the narrowing • Narrowing is not defined clearly as reduction of CSA or reduction in diameter
Zhang et al (2003)[37]	> 50% expiratory reduction in CSA	• Only for tracheal collapse • Low-dose CT imaging (40-80 mA) was just as accurate as the standard dose (240-280 mA) • Used paired inspiratory-dynamic expiratory CT imaging
Boiselle et al (2009)[34]	> 50% expiratory reduction in CSA	• Only for tracheal collapse in healthy volunteers • Used low-dose paired inspiratory-dynamic expiratory CT imaging • 80% of healthy study participants met the criteria for abnormal collapse
Boiselle et al (2012)[38]	> 80% expiratory reduction in CSA	• Only for tracheal collapse in patients with COPD • Used low-dose paired inspiratory-dynamic expiratory CT imaging
Murgu and Holt (2013)[33]	FEMOS system: functional assessment (F), degree of airway wall lesions (E), morphologic features (M), cause or origin (O), and degree of airway collapse (S)	• Evaluation content is comprehensive, but it is complex to use • The diagnostic criterion for ECAC is > 50% reduction in CSA, which cannot fully distinguish healthy individuals
Trujillo et al (2023)[32]	• EDAC severity scoring system: 0 points (< 70%), 1 point (70%-79%), 2 points (80%-89%), and 3 points (> 90%) • A total score of 9 being the threshold for severe EDAC requiring further intervention	• Used dynamic bronchoscopic estimations • Only used for EDAC, not including TBM

BM = bronchomalacia; CSA = cross-sectional area; ECAC = expiratory central airway collapse; EDAC = excessive dynamic airway collapse; TBM = tracheobronchomalacia; TM = tracheomalacia.

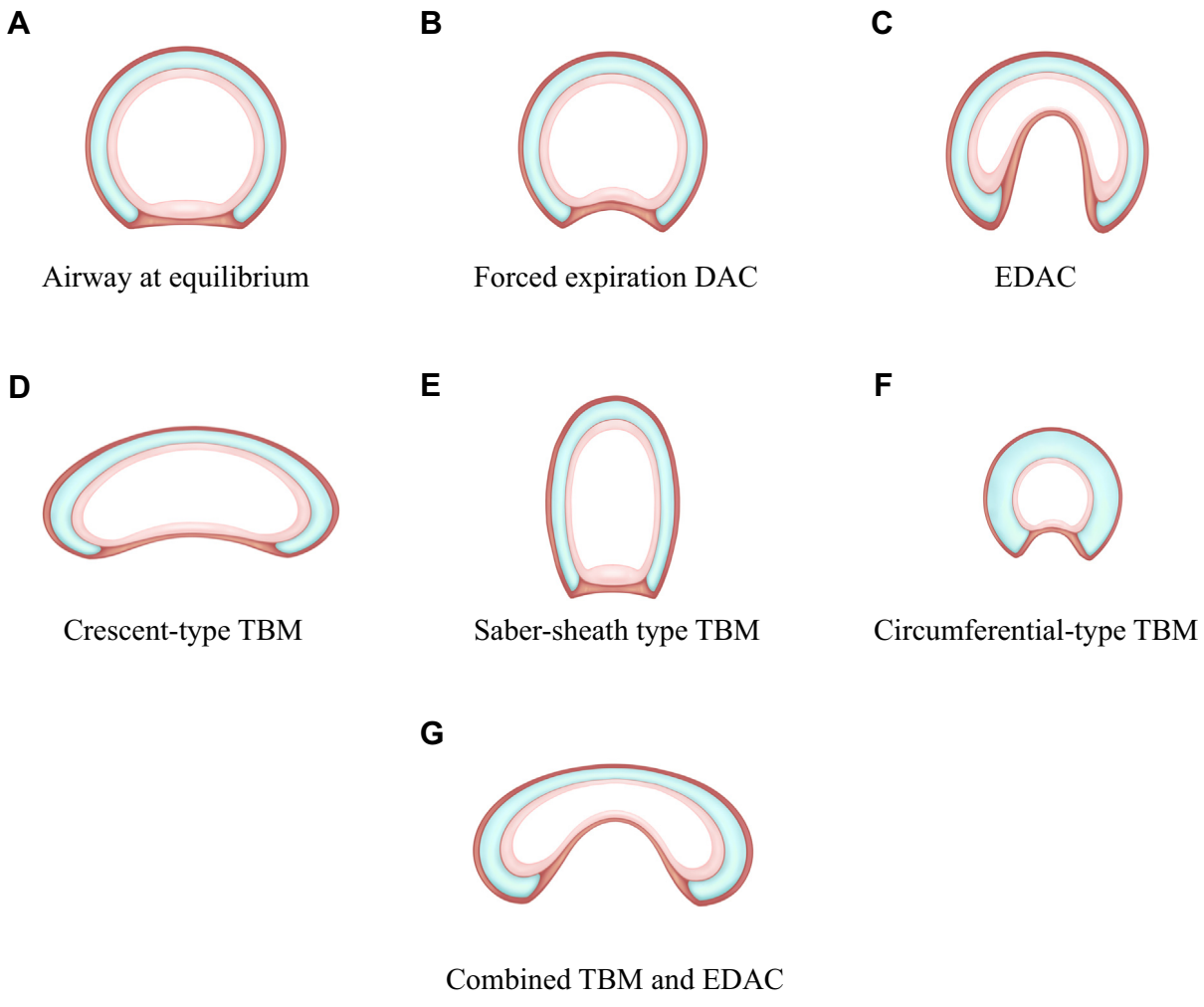

Figure 3 – *A-G, Schematic diagram showing a healthy airway and COPD-associated expiratory central airway collapse: healthy airway (A), healthy airway collapse during forced expiration (B), EDAC (C), crescent TBM (D), saber-sheath TBM (E), circumferential TBM (F), and TBM and EDAC (G). DAC, dynamic airway collapse; EDAC = excessive dynamic airway collapse; TBM = tracheobronchomalacia.*

needed.[1,50-52] The diagnosis and treatment flowchart is presented in Figure 7. The specific treatment content of this manuscript is shown in Table 4.

Noninvasive Ventilation: This treatment method provides positive airway pressure that prevents central airway collapse, alleviates breathing difficulties, and improves secretion clearance and ventilation by acting as a pneumatic stent.[53] Patout et al[10] treated a 62-year-old patient with COPD, tracheobronchomalacia, and OSA using a portable CPAP device. A pressure of 4 cm H_2O increased the 6-minute walking distance by 60 m. However, the test could not be completed when using a pressure of 10 cm H_2O, because the patient experienced severe breathing difficulties; further evaluation of the clinical response and pressure setting for CPAP therefore is required. Olley et al[54] reported a patient with EDAC who consistently experienced severe cough and sleep disorder whose quality and duration of sleep, daytime symptoms, and QoL were improved significantly after nocturnal CPAP therapy. Pradeep et al[55] treated a 70-year-old patient with severe OSA and tracheobronchomalacia who could not tolerate CPAP with nocturnal bi-level positive airway pressure (BiPAP) ventilation (inspiratory positive airway pressure [PAP], 16 cm H_2O; expiratory PAP, 4 cm H_2O), which alleviated airway collapse and significantly improved symptoms. COPD often involves endogenous PAP, which can be counteracted by expiratory positive airway pressure in BiPAP mode, thereby improving breathing difficulties. Therefore, BiPAP is used widely in patients with COPD. For COPD-associated ECAC, BiPAP may also be more effective; however, large-scale randomized controlled trials (RCTs) are required to verify this.

Figure 4 – *A-P, Images showing bronchoscopy manifestations of healthy airways and COPD-associated expiratory central airway collapse: healthy airway (in white light mode) (A, B), healthy airway (narrow band imaging) (C), healthy airway (autofluorescence imaging) (D), tracheomalacia with almost complete disappearance of the cartilage ring (E), saber-sheath-like tracheomalacia with deformation of the cartilage ring accompanied by mucosal inflammation (F), saber-sheath-like tracheomalacia (inspiratory phase) (G), saber-sheath-like tracheomalacia (expiratory phase) (H), bronchomalacia of right main bronchus with almost complete disappearance of the cartilage ring (I), bronchomalacia of left main bronchus with almost complete disappearance of the cartilage ring (J), crescent bronchomalacia of right main bronchus (inspiratory phase) (K), lumen of right main bronchus with almost complete occlusion (expiratory phase) (L), crescent bronchomalacia of left main bronchus (inspiratory phase) (M), lumen of left main bronchus with almost complete occlusion (expiratory phase) (N), crescent bronchomalacia of middle segment bronchus of right lung (inspiratory phase) (O), and gap-like stenosis of middle segment bronchus of right lung (expiratory phase) (P).*

Airway Stents: This treatment method implants a metal or silicone stent into the central airway through a flexible bronchoscope or rigid bronchoscope to stabilize the airway, improving airway collapse and respiratory symptoms.

Stents as a Therapeutic Trial: A 2-week stent trial should be considered before operation of tracheobronchoplasty to ensure which patient is suitable for this procedure. Only the patients who demonstrate symptomatic and objective improvements during the stent trial can be considered for tracheobronchoplasty. Airway stent implantation can be considered for patients with severe tracheobronchomalacia and obvious symptoms because it can improve symptoms significantly; however, it represents only a temporary solution.[2] Previous studies[2,56,57] have reported that 60% to 75% of patients with severe ECAC exhibit

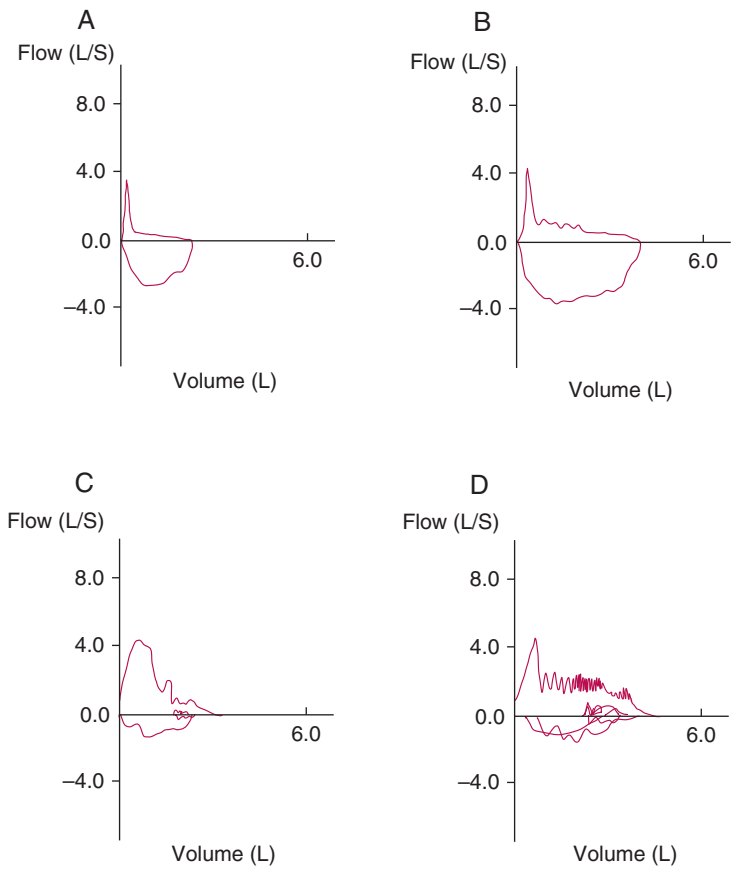

Figure 5 – *Graphs showing partial characteristic findings in flow-volume loops in COPD-associated expiratory central airway collapse. A, Inflection point pattern showing sudden decrease in peak expiratory flow, defined as 50% decrease within 25% of FVC. B, Biphasic morphologic features show rapid peak and decline in expiratory flow, followed by prolonged plateau extending throughout most of expiratory maneuver. C, Notched expiratory loop shows rapid mid-expiratory dip and return of flow, without other indications of cough, and is reproducible in several maneuvers. D, Expiratory oscillations characterized by reproducible large-amplitude, high-frequency oscillations over much of the expiratory loop.*

improvement in symptoms after the stent trial and then undergo surgical tracheobronchoplasty. If patients with ECAC do not show significant improvements in symptoms, lung function, or QoL after stent trial, the benefits of tracheobronchoplasty may be limited. The reasons for the failure of a stent trial are complex, with common causes including serious comorbidities and inappropriate stent size. Therefore, other treatments need to be considered (Fig 7).

Stent for Curative Intent: Although long-term implantation of a stent may lead to various serious complications, it is an important intervention to maintain the stability of airway. Popilevsky et al[8] implanted 2 separate dynamic Y-shaped tracheal stents at different times in a patient with COPD and severe tracheobronchomalacia who declined other treatments. Although the patient's symptoms improved after stent implantation, both stents ruptured and were removed approximately 1 year after implantation. Finally, a silicone Dumon Y stent was deployed in the airway of this patient, and subsequent surveillance bronchoscopy revealed an intact and well-functioning stent. Thus far, no permanent stent has proven to be suitable for treatment of COPD-associated ECAC. For patients who have no other options but do benefit from a stent trial, long-term stent implantation can be considered after a risk-benefit assessment.

Types of Stents: Currently, although various types of stents are available for treatment of COPD-associated ECAC, each has its own advantages and disadvantages. The risks of breakage and bleeding are lower with silicone stents than with metal stents; however, the risks of displacement and secretion-drainage disorders are higher. Currently, metal stents are not recommended for benign airway stenosis such as ECAC. Dalar et al[58] implanted silicone stents in 10 patients with tracheobronchomalacia. Three patients with stent displacement and 5 patients with severe

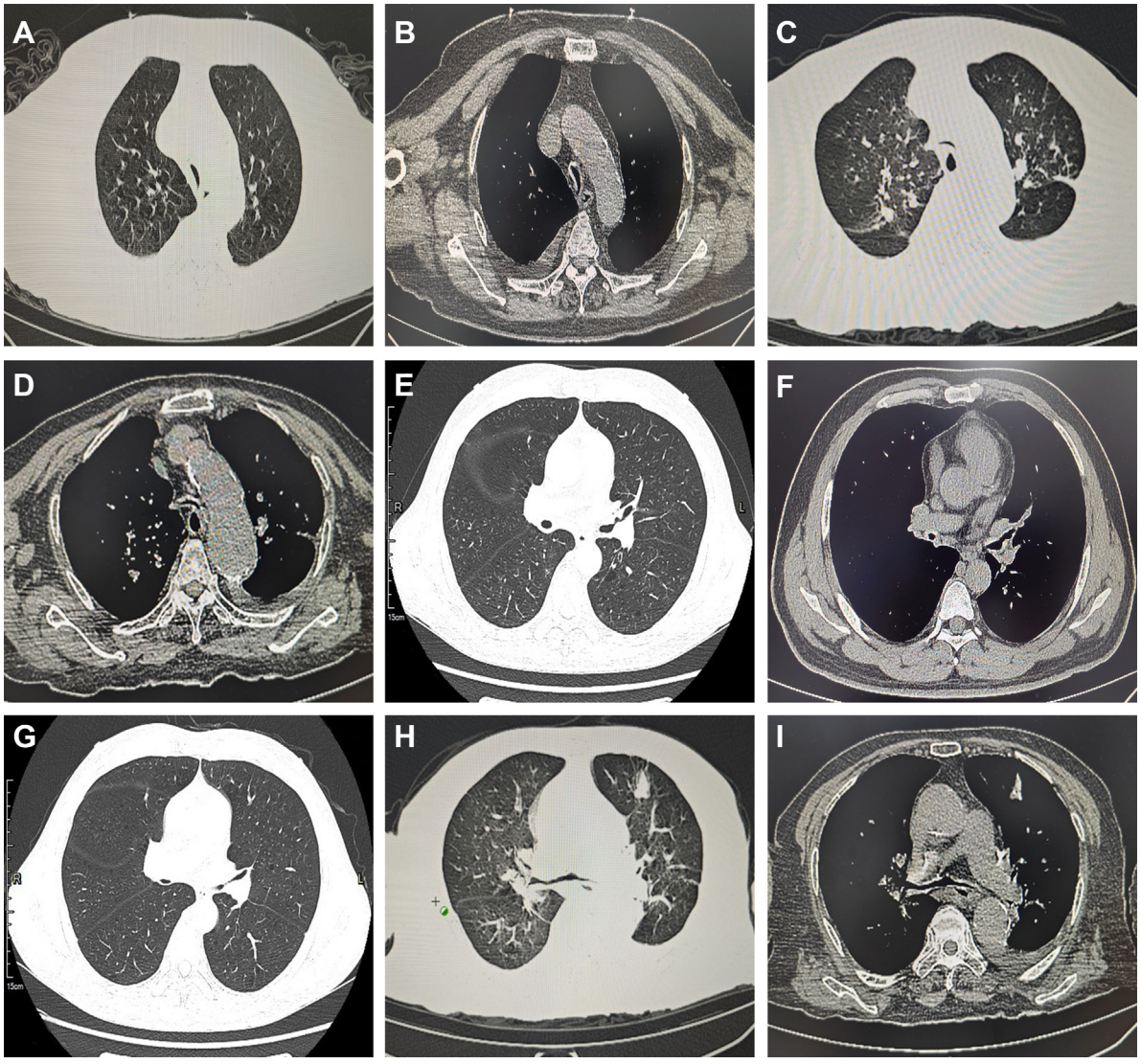

Figure 6 – *A-I, Chest CT images showing manifestations of COPD-associated expiratory central airway collapse: saber-sheath tracheomalacia (A); mediastinal window showing a significant thickening of the tracheal wall, narrowing of lumen, and airway remodeling (B); crescent tracheomalacia (C); mediastinal window showing a significant thickening of the tracheal wall, narrowing of lumen, and airway remodeling (D); no obvious abnormalities in the middle segment bronchus of right lung (inspiratory phase) (E); mediastinal window showing a significant thickening of the middle segment bronchus wall of the right lung, narrowing of lumen, and airway remodeling (F); compared with inhalation, lumen of the middle segment bronchus of right lung is narrowed significantly during exhalation (G); gap-like stenosis of bilateral main bronchus (inspiratory phase) (H); and mediastinal window showing a significant thickening of the bilateral main bronchus wall, narrowing of the lumen, and airway remodeling (I).*

secretion-drainage disorders underwent stent removal; only 2 patients experienced significant clinical benefits. Some patients with tracheobronchomalacia may have irregular airways, and therefore the use of three-demensional printed stents has been proposed. Schweiger et al[59] reported cases of 2 patients with tracheobronchomalacia who had previously undergone tracheobronchoplasty. The surgical benefits of tracheobronchoplasty decreased over time and symptoms worsened. These symptoms were relieved by the implantation of 3-dimensional printed silicone stents. However, the long-term benefits of 3-dimensional printed stents remain to be determined.

Surgical Procedures: Surgical treatment methods play a very important role in maintaining the stability of central airway by tracheotomizing and implanting an artificial tube, removing locally collapsed trachea, or plicating the redundant posterior membranous wall with a mesh to ameliorate symptoms and improve lung function.

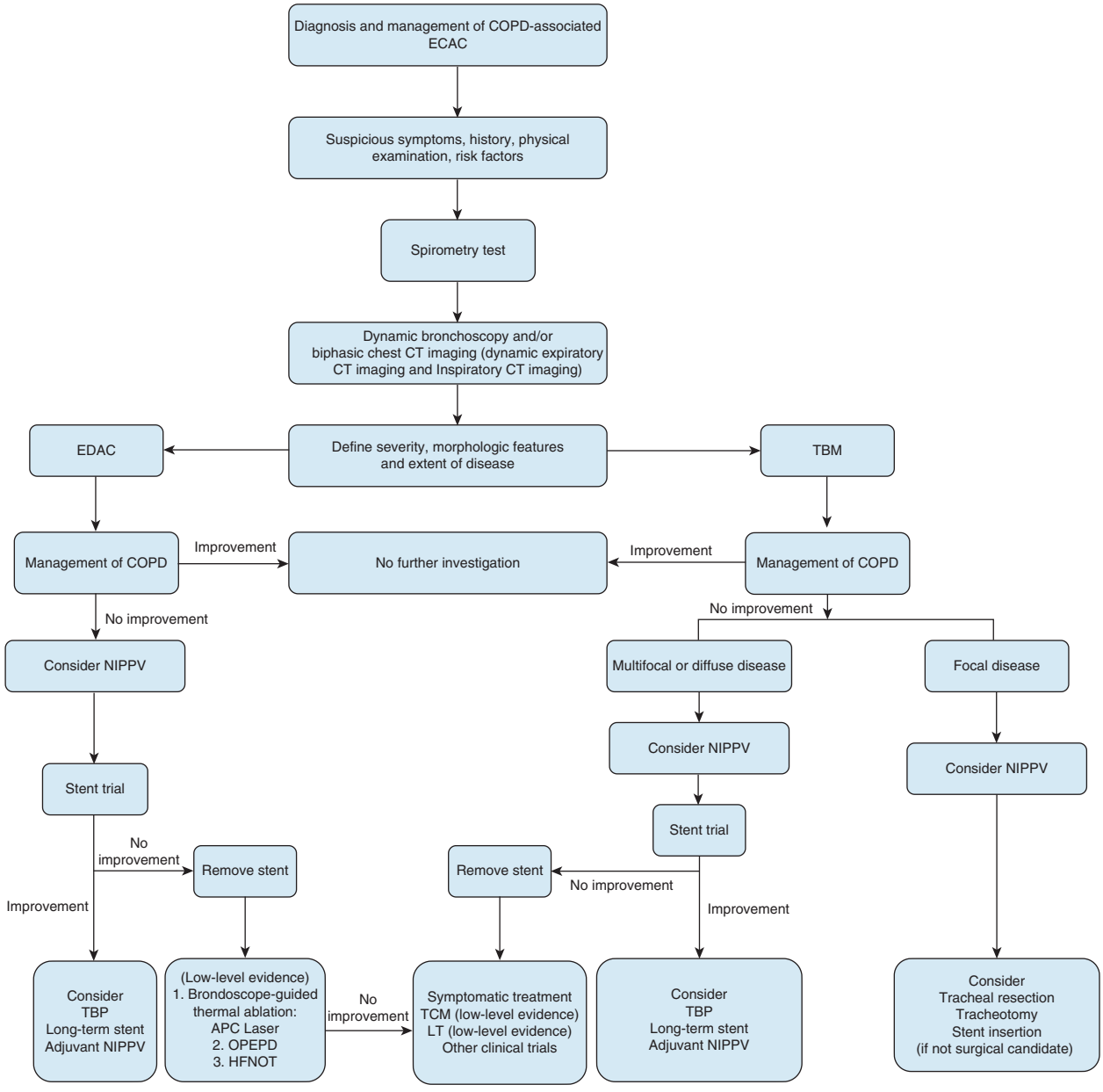

Figure 7 – *Flowchart showing diagnosis and treatment of COPD-associated ECAC. APC = argon plasma coagulation; ECAC = expiratory central airway collapse; EDAC = excessive dynamic airway collapse; HFNOT = high-flow nasal oxygen therapy; LT = lung transplantation; NIPPV = noninvasive positive pressure ventilation; OPEPD = oral positive expiratory pressure device; TBM = tracheobronchomalacia; TBP = tracheobronchoplasty; TCM = traditional Chinese medicine.*

Surgical procedures mainly include tracheotomy, tracheal resection, and tracheobronchoplasty.

Tracheotomy and Tracheal Resection: Tracheotomy keeps the collapsed airway open, providing an effective artificial airway.[60] However, this procedure is associated with numerous complications such as extubation difficulty, tracheal constriction and stenosis, tracheal injury, secondary tracheobronchomalacia, and recurrent respiratory infections, and therefore can be used only as a temporary measure.[61] Tracheal resection is suitable only for focal tracheobronchomalacia, because it is ineffective for widespread airway collapse.

Open Tracheobronchoplasty: Tracheobronchoplasty is a commonly used central airway stabilization surgery for the treatment of tracheobronchomalacia, which mainly includes open tracheobronchoplasty and robot-assisted tracheobronchoplasty (R-TBP). Tracheobronchoplasty has been proven to be a successful treatment method

TABLE 4] Treatment of COPD-Associated ECAC

Category	Reference	Patient Selection	No. of Participants	Trial Design	Intervention	Outcomes
Noninvasive ventilation	Funes-Ferrada et al (2024)[53]	• TBM • Comorbidities: right pneumonectomy and SCC	75-year-old woman	Case report	CPAP	Improvement in symptoms and functional capacity
	Patout et al (2016)[10]	• TBM • Comorbidities: COPD, OSA	62-year-old man	Case report	Portable CPAP	4 cm H_2O: improvement in 6MWT; 10 cm H_2O: inability to tolerate this test
	Olley et al (2023)[54]	• TBM • Comorbidities: asthma, LRTI, chronic rhinosinusitis, septoplasty, breast cancer, primary lung cancer, left upper lobectomy, right knee replacement, cervical spinal fusion	63-year-old woman	Case report	Nocturnal CPAP	Improvement in quality and duration of sleep, daytime symptoms, and quality of life
	Pradeep et al (2003)[55]	• TBM • Comorbidities: DM, HP, OSA, RF	70-year-old man	Case report	BiPAP (during sleep)	CPAP: inability to tolerate; BiPAP: improvement
Airway stent	Ernst et al (2011)[2]	• TBM • Comorbidities: COPD	94	Cohort study	Silicone stents	49% patients show improvement in symptoms
	Popilevsky et al (2012)[8]	• TBM • Comorbidities: COPD, GERD	60-year-old man	Case report	Dynamic Y-shaped tracheal stents	Improvement; stents ruptured and were removed 1 year after implantation
	Dalar et al (2016)[58]	• TBM • Comorbidities: COPD, 6; HP, 5; DM, 1; CHF, 2; malignancy, 1; OSA plus COPD, 1	10 (median [SD] age, 65.07 [13.19] y)	Observational study	Silicone stents	Only 2 patients showed improvement in symptoms; stents were removed from 8 patients because of displacement poor sputum drainage
	Schweiger et al (2016)[59]	• EDAC • Comorbidities: COPD	2 (69-year-old and 71-year-old men)	Case report	3D printed silicone stents	Benefits of TBP decreased over time and symptoms worsened; relieved by the implantation of 3D printed silicone stents
Tracheobronchoplasty	Majid et al (2008)[9]	• TBM • Comorbidities: COPD, 11; asthma, 9; MKS, 4	33 (20 men,13 women; median age, 61 y)	Observational study	Open TBP with polypropylene mesh	Improvement in quality of life, dyspnea scores, functional status scores, and exercise capacity

(Continued)

TABLE 4] *(Continued)*

Category	Reference	Patient Selection	No. of Participants	Trial Design	Intervention	Outcomes
	Buitrago et al (2018)[62]	• TBM • Comorbidities: CAD, 29; COPD, 67; CHF, 14; DM, 42; HP, 71; MI, 14; PAD, 9; VTE, 21	161 (58 men, 103 women; median age, 58 y)	Cohort study	Open TBP with polypropylene mesh	Postoperative morbidity, 47%; severe complications, 24%; 2 patients died in hospital; median ICU stay, 4 d; total hospital stay, 8 d
	Buitrago et al (2023)[63]	• TBM • Comorbidities: COPD, 19; asthma, 25; OSA, 22; GERD, 32; DM, 16	61 (12 men, 49 women; median age, 58 y)	Cohort study	Open TBP with polypropylene mesh	Show durable effects on airway anatomic features, functional status, and quality of life
	Bakhos et al (2022)[64]	• TBM • Comorbidities: COPD, 2; asthma, 4; OSA, 4; GERD, 4; MKS, 1; recurrent bronchitis, 1	8 (3 men, 5 women; median age, 58 y)	Observational study	• 5 patients: open TBP with polypropylene mesh • 3 patients: open TBP with polypropylene mesh	Improvement in lung function and CT imaging results
	Lazzaro et al (2019)[66]	• TBM • Comorbidities: asthma, 88%; COPD, 52%; GERD, 85%; HP, 52%; DM, 26%; CD, 14%; prior chest surgery, 14%	42 (12 men, 30 women; median age, 66 y)	Retrospective study	Robot-assisted TBP with polypropylene mesh	Improvement in lung function and quality of life questionnaire scores
	Lazzaro et al (2022)[67]	• TBM • Comorbidities: asthma, 37; COPD, 22; OSA, 35; GERD, 36; HP, 22; DM, 11; CD, 6; prior chest surgery, 6	42 (12 men, 30 women; median age, 66.84 y)	Retrospective study	Robot-assisted TBP with polypropylene mesh	Improvement in quality of life and postoperative pulmonary function
TCM	Zhou et al (2019)[68]	• TBM • Comorbidities: COPD, 30; CHF, 25; RF, 27; PIF, 10; lung cancer, 22; bronchiectasis, 4; pulmonary TB, 2; HP, 8; arrhythmia, 4; DM, 2; DVT, 1; SSS and pacemaker implantation, 1	60 (50 men, 10 women; median age, 72.8 y)	Observational study	TCM: Tiaobu Feishen formula	Improvement in mMRC, CAT, and pulmonary function

(Continued)

TABLE 4] *(Continued)*

Category	Reference	Patient Selection	No. of Participants	Trial Design	Intervention	Outcomes
	Zhou et al (2022)[51,69]	TBM and COPD	COPD-associated TBM cell model	Ex vivo pilot study	TCM: Tiaobu Feishen decoction	Inhibiting the caveolin-1-p38 MAPK signaling pathway, reducing chondrocyte degeneration
Bronchoscopy-guided thermal ablation	de Lima et al (2020)[70]	ECAC	4 sheep tracheal tissue	Ex vivo pilot study	EC, RFA, KTP, APC	APC at high power settings may be the most suitable method
	Gangadharan et al (2023)[52]	ECAC	None	Review	APC, YAP, KTP	May be a promising alternative to traditional surgery
Other PEP therapies	Zafa et al (2021)[71]	EDAC and emphysema	31-year-old woman	Case report	o-PEP	Reduced airway collapse and improved dyspnea, quality of life, and exertional desaturation
	Park et al (2015)[72]	EDAC, DM, and diastolic heart failure	80-year-old woman	Case report	Tracheostomy and HFNOT	Improvement in symptoms and successful removal of the tracheal intubation
Lung transplantation	Eberlein et al (2013)[73]	• TBM • Comorbidities: MKS and severe bronchiectasis	51-year-old man	Case report	Double lung transplantation	Long-term survival and significantly improvement in quality of life
	Lehr et al (2016)[74]	TBM and COPD	None	Case report	Double lung transplantation	Improvement in symptoms and lung function
	Singh et al (2019)[75]	COPD and EDAC	8 (6 men, 2 women; median age, 60.3 y)	Retrospective study	Double lung transplantation	No EDAC; improvement in lung function

3D = 3-dimensional; 6MWT = 6-minute walk test; APC = argon plasma coagulation; BiPAP = bi-level positive airway pressure; CAD = coronary artery disease; CAT = COPD Assessment Test; CD = cardiovascular disease; CHF = congestive heart failure; DM = diabetes mellitus; EC = electrocautery; ECAC = expiratory central airway collapse; EDAC = excessive dynamic airway collapse; GERD = gastroesophageal reflux disorder; HFNOT = high-flow nasal oxygen therapy; HP = hypertension; KTP = potassium titanyl phosphate; LRTI = lower respiratory tract infection; MAPK = mitogen-activated protein kinase; MI = myocardial infarction; mMRC = modified Medical Research Council; MKS = Mounier-Kuhn syndrome; o-PEP = oral positive expiratory pressure; PAD = peripheral arterial disease; PIF = pulmonary interstitial fibrosis; RFA = radiofrequency ablation; RF = respiratory failure; SCC = squamous cell carcinoma; SSS = sick sinus syndrome; TBM = tracheobronchomalacia; TBP = tracheobronchoplasty; TCM = traditional Chinese medicine; YAP = holmium and yttrium aluminum perovskite.

with a positive impact in patients' lives. Only patients who benefit from short-term stent placement and have severe symptoms are suitable for tracheobronchoplasty.[9] Buitrago et al[57] reported that approximately 80% of patients with tracheobronchomalacia who benefit from stent trials experience continued improvement in symptoms, QoL, and exercise capacity after tracheobronchoplasty. The reasons for the failure of tracheobronchoplasty are complex, with common causes including serious comorbidities and patient loss to follow-up. Traditional tracheobronchoplasty requires open thoracotomy and may have more perioperative complications. Buitrago et al[62] reported their experience with 161 patients who underwent open tracheobronchoplasty from 2002 through 2016. This study showed that 38 patients (24%) experienced severe complications, of whom 27 patients (17%) experienced respiratory failure and two patient died in hospital. Although that study has shown that open tracheobronchoplasty has many perioperative complications, the mortality rate is very low. At present, relatively few studies have reported on long-term follow-up after open tracheobronchoplasty surgery. A cohort study of 61 patients with a 5-year follow-up showed that tracheobronchoplasty had durable effects on airway anatomic features, functional status, and QoL in carefully selected patients with severe excessive central airway collapse.[63]

Robot-Assisted Tracheobronchoplasty: R-TBP has significant advantages over open tracheobronchoplasty, including better exposure to the left main bronchus, good visualization effect throughout the operation, and significant ergonomic benefits for operating surgeon, and seems to be associated with a shorter hospital stay and lower morbidity.[64] Previous studies have demonstrated that R-TBP is safe and is associated with improvements in pulmonary function and subjective improvement in QoL.[65] Lazzaro et al[66] reported the outcomes of the first series of R-TBP procedures for the treatment of tracheobronchomalacia. This study showed that R-TBP could be performed with low morbidity and mortality. Early follow-up revealed significant improvement in pulmonary function and high patient satisfaction when compared with preoperative baseline characteristics. Thus far, this is the largest R-TBP series in the literature. A recent follow-up study showed that R-TBP not only was associated with low intermediate-term (median follow-up is 40 months) mortality, but also resulted in significant improvement in QoL and postoperative pulmonary function.[67] Therefore, further evaluation of the long-term efficacy of open tracheobronchoplasty or R-TBP on halting pathologic progression of tracheobronchomalacia and establishing the long-term impact of tracheobronchoplasty on symptomatic and functional improvements is needed.

Other Therapies: Although Tiaobu Feishen formula (a traditional Chinese herbs prescription),[51,68,69] argon plasma coagulation,[52,70] laser therapy,[52] oral positive expiratory pressure device treatment,[71] high-flow nasal oxygen therapy,[72] and lung transplantation[73-75] have shown efficacy in COPD-associated ECAC treatment, these studies mainly are low evidence-based case reports. In the future, large-sample RCTs need to be evaluated further for the exact role of these therapies and complications.

Future Directions

In the future, it is important to develop consistent definitions of COPD-associated ECAC based on clinical and diagnostic criteria. Epidemiologic studies of COPD-associated ECAC are required to provide a basis for health decision-making and disease prevention and management. The effects of noninvasive PAP ventilation on severe tracheobronchomalacia remain unclear, and clinical trials are required to verify them. In the future, combining the latest developments in materials science and manufacturing may improve the material composition, shape, construction processes, and biocompatibility of stents. Tracheobronchoplasty has a definite therapeutic effect in patients with severe tracheobronchomalacia; however, perioperative complications remain a serious issue, and observation of its long-term efficacy is required. In the future, RCTs of different therapies using patient-centered outcomes, cost-effective analysis on different interventions, and consensus guidelines on COPD-associated ECAC are needed urgently.

Summary

COPD-associated ECAC is a frequently overlooked benign obstructive airway disease, and its pathologic mechanisms, diagnosis, and management are full of challenges. Noninvasive ventilation, airway stents, and tracheobronchoplasty remain the main interventions. Traditional Chinese medicine and other new therapies have shown potential with limited evidence. In the future, RCTs of different therapies and consensus on COPD-associated ECAC are needed urgently.

Funding/Support

This work was supported by the National Natural Science Foundation of China [Grant 81904177]. The 2023 Xinglin Scholars Scientific Research Promotion Plan of Chengdu University of Traditional Chinese Medicine [Grant QJRC2023004], the Hundred Talents Plan Project of Hospital of Chengdu University of Traditional Chinese Medicine [Grant 20-Q07], the Science and Technology Development Fund of Hospital of Chengdu University of Traditional Chinese Medicine [Grant 22ZL03], and the Sichuan Medical Research Youth Innovation Project [Grant Q23035].

Financial/Nonfinancial Disclosures

None declared.

Acknowledgments

Author contributions: C. H. and Q. X. designed the outline of the study. P. Z., W. Y., and W. Z. conceived the study and drafted and revised the manuscript. J. M. participated in the drawing of partial figures in the manuscript. All authors contributed toward data analysis, drafting, and critically revising the article; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Role of sponsors: The sponsor had no role in the design of the study, the collection and analysis of the data, or the preparation of the manuscript.

References

1. Aslam A, De Luis Cardenas J, Morrison RJ, et al. Tracheobronchomalacia and excessive dynamic airway collapse: current concepts and future directions. *Radiographics*. 2022;42(4):1012-1027.
2. Ernst A, Odell DD, Michaud G, Majid A, Herth FFJ, Gangadharan SP. Central airway stabilization for tracheobronchomalacia improves quality of life in patients with COPD. *Chest*. 2011;140(5):1162-1168.
3. Kandaswamy C, Balasubramanian V. Review of adult tracheomalacia and its relationship with chronic obstructive pulmonary disease. *Curr Opin Pulm Med*. 2009;15(2):113-119.
4. Heussel CP, Ley S, Biedermann A, et al. Respiratory lumenal change of the pharynx and trachea in normal subjects and COPD patients: assessment by cine-MRI. *Eur Radiol*. 2004;14(12):2188-2197.
5. Safiri SA-O, Carson-Chahhoud K, Noori M, et al. Burden of chronic obstructive pulmonary disease and its attributable risk factors in 204 countries and territories, 1990-2019: results from the Global Burden of Disease Study 2019. *BMJ*. 2022 (1756-1833[electronic]):378:e069679.
6. Bhatt SP, Terry NL, Nath H, et al. Association between expiratory central airway collapse and respiratory outcomes among smokers. *JAMA*. 2016;315(5):498-505.
7. Carden K, Boiselle P, Waltz D, Ernst A. Tracheomalacia and tracheobronchomalacia in children and adults: an in-depth review. *Chest*. 2005;127(3):984-1005.
8. Popilevsky F, Al-Ajam MR, Ly V, Sanchez LD, Cutaia M. Dynamic Y stent fractures in crescentic tracheobronchomalacia. *J Bronchology Interv Pulmonol*. 2012;19(3):206-210.
9. Majid A, Guerrero J, Gangadharan S, et al. Tracheobronchoplasty for severe tracheobronchomalacia: a prospective outcome analysis. *Chest*. 2008;134(4):801-807.
10. Patout M, Mylott L, Kent R, Arbane G, Murphy PB, Hart N. Trial of portable continuous positive airway pressure for the management of tracheobronchomalacia. *Am J Respir Crit Care Med*. 2016;193(10):e57.
11. Kamran A, Jennings RW. Tracheomalacia and tracheobronchomalacia in pediatrics: an overview of evaluation, medical management, and surgical treatment. *Front Pediatr*. 2019;(7):512.
12. Majid A, Kheir F, Alape D, et al. The prevalence of gastroesophageal reflux in patients with excessive central airway collapse. *Chest*. 2019;155(3):540-545.
13. Sverzellati N, Rastelli A, Chetta A, et al. Airway malacia in chronic obstructive pulmonary disease: prevalence, morphology and relationship with emphysema, bronchiectasis and bronchial wall thickening. *Eur Radiol*. 2009;19(7):1669-1678.
14. Shah V, Husta B, Mehta A, et al. Association between inhaled corticosteroids and tracheobronchomalacia. *Chest*. 2020;157(6):1426-1434.
15. Husta BC, Raoof S, Erzurum S, Mehta AC. Tracheobronchopathy from inhaled corticosteroids. *Chest*. 2017;152(6):1296-1305.
16. Chaddha U, Agrawal A, Maldonado F, Smaldone G, Murgu S. Excessive dynamic airway collapse in asthma and COPD: physiologic epiphenomenon or steroid-induced myopathy? *Chest*. 2020;158(6):2695-2696.
17. Lee EY,DL, Boiselle PM. Multidetector CT evaluation of tracheobronchomalacia. *Radiol Clin North Am*. 2009;47(2):261-269.
18. Hammond K, Ghori UK, Musani AI. Tracheobronchomalacia and excessive dynamic airway collapse. *Clin Chest Med*. 2018;39(1):223-228.
19. Inoue M, Hasegawa I, Nakano K, Yamaguchi K, Kuribayashi S. Incidence of tracheobronchomalacia associated with pulmonary emphysema: detection with paired inspiratory-expiratory multidetector computed tomography using a low-dose technique. *Jpn J Radiol*. 2009;27(8):303-308.
20. Loring SH, O'Donnell CR, Feller-Kopman DJ, Ernst A. Central airway mechanics and flow limitation in acquired tracheobronchomalacia. *Chest*. 2007;131(4):1118-1124.
21. Lee KS, Sun MRM, Ernst A, Feller-Kopman D, Majid A, Boiselle PM. Comparison of dynamic expiratory CT with bronchoscopy for diagnosing airway malacia: a pilot evaluation. *Chest*. 2007;131(3):758-764.
22. O'Donnell CR, Bankier AA, O'Donnell DH, Loring SH, Boiselle PM. Static end-expiratory and dynamic forced expiratory tracheal collapse in COPD. *Clin Radiol*. 2014;69(4):357-362.
23. Sindhwani G, Sodhi R, Saini M, Jethani V, Khanduri S, Singh B. Tracheobronchomalacia/excessive dynamic airway collapse in patients with chronic obstructive pulmonary disease with persistent expiratory wheeze: a pilot study. *Lung India*. 2016;33(4):381-384.
24. Represas-Represas C, Leiro-Fernández V, Mallo-Alonso R, Botana-Rial MI, Tilve-Gómez A, Fernández-Villar A. Excessive dynamic airway collapse in a small cohort of chronic obstructive pulmonary disease patients. *Ann Thorac Med*. 2015;10(2):118-122.
25. The GOLD Science Committee. Global strategy for prevention, diagnosis and management of COPD: 2024 Report. 2024. Global Initiative for Chronic Obstructive Lung Disease website. Accessed January 9, 2025. https://goldcopd.org/2024-gold-report/
26. Matus I, Richter W, Mani SB. Awareness, competencies, and practice patterns in tracheobronchomalacia: a survey of pulmonologists. *J Bronchology Interv Pulmonol*. 2016;23(2):131-137.
27. Choo EM, Seaman JC, Musani AI. Tracheomalacia/tracheobronchomalacia and hyperdynamic airway collapse. *Immunol Allergy Clin North Am*. 2013;33(1):23-34.
28. Rayl JE. Tracheobronchial collapse during cough. *Radiology*. 1965;85:87-92.
29. Jokinen K, Palva T, Sutinen S, Nuutinen J. Acquired tracheobronchomalacia. *Ann Clin Res*. 1977;9(2):52-57.
30. Johnson TH, Mikita JJ, Wilson RJ, Feist JH. Acquired tracheomalacia. *Radiology*. 1973;109(3):576-580.
31. Mair EA, Parsons DS. Pediatric tracheobronchomalacia and major airway collapse. *Ann Otol Rhinol Laryngol*. 1992;101(4):300-309.

32. Abia-Trujillo D, Yu Lee-Mateus A, Hernandez-Rojas D, et al. Excessive dynamic airway collapse severity scoring system: a call out for an overall severity determination. *J Bronchology Interv Pulmonol*. 2023;30(3):200-206.
33. Murgu S, Colt H. Tracheobronchomalacia and excessive dynamic airway collapse. *Clin Chest Med*. 2013;34(3):527-555.
34. Boiselle PM, O'Donnell CR, Bankier AA, et al. Tracheal collapsibility in healthy volunteers during forced expiration: assessment with multidetector CT. *Radiology*. 2009;252(1):255-262.
35. Nuutinen J. Acquired tracheobronchomalacia. A clinical study with bronchological correlations. *Ann Clin Res*. 1977;9(6):350-355.
36. Stern EJ, Graham CM, Webb WR, Gamsu G. Normal trachea during forced expiration: dynamic CT measurements. *Radiology*. 1993;187(1):27-31.
37. Zhang J, Hasegawa I, Feller-Kopman D, Boiselle PM. 2003 AUR Memorial Award. Dynamic expiratory volumetric CT imaging of the central airways: comparison of standard-dose and low-dose techniques. *Acad Radiol*. 2003;10(7):719-724.
38. Boiselle PM, Michaud G, Roberts DH, et al. Dynamic expiratory tracheal collapse in COPD: correlation with clinical and physiologic parameters. *Chest*. 2012;142(6):1539-1544.
39. Masaoka A, Yamakawa Y, Niwa H, et al. Pediatric and adult tracheobronchomalacia. *Eur J Cardiothorac Surg*. 1996;10(2):87-92.
40. Nuutinen J. Acquired tracheobronchomalacia. A clinical study with bronchological correlations. *Ann Clin Res*. 1977;9(6):350-355.
41. Ernst A, Majid A, Feller-Kopman D, et al. Airway stabilization with silicone stents for treating adult tracheobronchomalacia: a prospective observational study. *Chest*. 2007;132(2):609-616.
42. Nuutinen J. Acquired tracheobronchomalacia. *Eur J Respir Dis*. 1982;63(0106-4339):380-387.
43. Eberlein M, Bolukbas S, Reed RM. Pulmonary function and flow-volume loop patterns in patients with tracheobronchomalacia: is there an independent effect? *Respir Care*. 2014;59(2):e25.
44. Majid A, Sosa AF, Ernst A, et al. Pulmonary function and flow-volume loop patterns in patients with tracheobronchomalacia. *Respir Care*. 2013;58(9):1521-1526.
45. Lin S, Huang C, Feng Q, Yuan G. CT 3D imaging contrast bronchoscopy in diagnosis of airway malacia. *Int J Respir*. 2014;34(24):1855-1857.
46. Ferretti GR, Jankowski A, Perrin MA, et al. Multi-detector CT evaluation in patients suspected of tracheobronchomalacia: comparison of end-expiratory with dynamic expiratory volumetric acquisitions. *Eur J Radiol*. 2008;68(2):340-346.
47. Baroni RH, Feller-Kopman D, Nishino M, et al. Tracheobronchomalacia: comparison between end-expiratory and dynamic expiratory CT for evaluation of central airway collapse. *Radiology*. 2005;235(2):635-641.
48. Ciet P, Boiselle PM, Heidinger B, et al. Cine MRI of tracheal dynamics in healthy volunteers and patients with tracheobronchomalacia. *AJR Am J Roentgenol*. 2017;209(4):757-761.
49. Deryk S, Nieboer K, Ceulemans G, Bossuyt A, Vanhove C, Everaert H. Tracheobronchomalacia incidentally detected on Tc-99m ventilation/perfusion SPECT. *Clin Nucl Med*. 2009;34(9):622-624.
50. Wang JW, Jiang SH. [Tracheobronchomalacia and excessive dynamic airway collapse]. *Zhonghua Jie He He Hu Xi Za Zhi*. 2017;40(6):469-472.
51. Zhou P, Yu W, Zhang C, et al. Tiao-bu-fei-shen formula promotes downregulation of the caveolin 1-p38 MAPK signaling pathway in COPD: associated tracheobronchomalacia cell model. *J Ethnopharmacol*. 2022;293:115256.
52. Gangadharan SP, Mathew F. Thermoablative techniques to treat excessive central airway collapse. *Thorac Surg Clin*. 2023;33(3):299-308.
53. Funes-Ferrada R, Barrios-Ruiz A, Lee-Mateus Yu, Johnson MM, Fernandez-Bussy S, Abia-Trujillo D. Long-term pneumatic stenting with positive expiratory pressure therapy for severe expiratory central airway collapse. *Respirol Case Rep*. 2024;12(5):e01367.
54. Olley L, Steier J, Kaltsakas G. Nocturnal continuous positive airway pressure offers symptomatic benefit in excessive dynamic airway collapse despite normal sleep study. *J Thorac Dis*. 2023;15(2):829-834.
55. Pradeep NP, Ayub II, Krishnaswamy M, Periakaruppan G. Bilevel positive airway pressure in tracheobronchomalacia. *BMJ Case Rep*. 2021;14(10):e246331.
56. Gangadharan SP, Bakhos CT, Majid A, et al. Technical aspects and outcomes of tracheobronchoplasty for severe tracheobronchomalacia. *Ann Thorac Surg*. 2011;91(5):1574-1580.
57. Buitrago DH, Wilson JL, Parikh M, Majid A, Gangadharan SP. Current concepts in severe adult tracheobronchomalacia: evaluation and treatment. *J Thorac Dis*. 2017;9(1):E57-E66.
58. Dalar L, Tural Onur S, Ozdemir C, Sokucu SN, Karasulu AL, Altin S. Is silicone stent insertion a clinically useful option for tracheobronchomalacia? *Turk J Med Sci*. 2016;46(2):437-442.
59. Schweiger T, Gildea TR, Prosch H, Lang G, Klepetko W, Hoetzenecker K. Patient-specific, 3-dimensionally engineered silicone Y-stents in tracheobronchomalacia: clinical experience with a novel type of airway stent. *J Thorac Cardiovasc Surg*. 2018;156(5):2019-2021.
60. Liu YJ, Zhen KF, Tang XY, Jiang T, Li XF, Zhao JB. Treatment and progress of tracheobronchomalacia. *Chin J Thorac Surg*. 2020;7(03):186-190.
61. Mair EA, Parsons DS, Lally KP. Treatment of severe bronchomalacia with expanding endobronchial stents. *Arch Otolaryngol Head Neck Surg*. 1990;116(9):1087-1090.
62. Buitrago DH, Majid A, Alape DE, et al. Single-center experience of tracheobronchoplasty for tracheobronchomalacia: perioperative outcomes. *Ann Thorac Surg*. 2018;106(3):909-915.
63. Buitrago DH, Majid A, Wilson JL, et al. Tracheobronchoplasty yields long-term anatomy, function, and quality of life improvement for patients with severe excessive central airway collapse. *J Thorac Cardiovasc Surg*. 2023;165(2):518-525.
64. Bakhos CT, Magarinos J, Bent D, Petrov R, Abbas AE. Tracheobronchoplasty for tracheobronchomalacia. *J Vis Surg*. 2022;8:15.
65. Lazzaro R, Inra ML. Tracheobronchoplasty: indications and best approaches. *Thorac Surg Clin*. 2023;33(2):141-147.
66. Lazzaro R, Patton B, Lee P, et al. First series of minimally invasive, robot-assisted tracheobronchoplasty with mesh for severe tracheobronchomalacia. *J Thorac Cardiovasc Surg*. 2019;157(2):791-800.
67. Lazzaro RS, Patton BD, Wasserman GA, et al. Robotic-assisted tracheobronchoplasty: quality of life and pulmonary function assessment on intermediate follow-up. *J Thorac Cardiovasc Surg*. 2022 Jul;164(1):278-286.
68. Zhou P, Yu W, Chen K, Tang W. Effect of Tiaobufeishen recipe on pulmonary function and quality of life in patients with chronic obstructive pulmonary disease complicated with tracheobronchomalacia. *J Chengdu Univ Tradit Chin Med*. 2019;42(1):45-50.
69. Zhou P, Yu W, Chen K, et al. Effect of the tiaobufeishen decoction on caveolin-1-p38 MAPK signaling pathway and mechanism of improving the tracheobronchomalacia in chronic obstructive pulmonary disease. *TMR Integr Med*. 2019;3:e19002.
70. de Lima A, Vidal B, Kheir F, et al. Thermoablative techniques for excessive central airway collapse: an ex vivo pilot study on sheep tracheal tissue. *J Bronchology Interv Pulmonol*. 2020;27(3):195-199.
71. Zafar MA, Sengupta R, Bates A, et al. Oral positive expiratory pressure device for excessive dynamic airway collapse caused by emphysema. *Chest*. 2021;160(4):e333-e337.

72. Park J, Lee YJ, Kim SJ, et al. Successful high flow nasal oxygen therapy for excessive dynamic airway collapse: a case report. *Tuberc Respir Dis (Seoul)*. 2015;78(4):455-458.

73. Eberlein M, Geist LJ, Mullan BF, Parekh KR, Klesney-Tait JA. Long-term success after bilateral lung transplantation for Mounier-Kuhn syndrome: a physiological description. *Ann Am Thorac Soc*. 2013;10(5):534-537.

74. Lehr CJ, Ali SR, Mehta AC. The role of lung transplantation in excessive dynamic collapse. *J Heart Lung Transplant*. 2016;35(5):692-693.

75. Singh J, Sese D, Lehr CJ, Pichurko B, McCurry K, Mehta AC. Effect of bilateral lung transplantation on excessive dynamic airway collapse. *Clin Transplant*. 2019;33(6):e13578.