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REVIEW

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A review on diagnostic assessments of tracheal stenosis

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Abstract

Tracheal stenosis (TS) is a pathological condition characterized by a reduction in the trachea diameter. It is a common complication after prolonged endotracheal intubation but may also arise from autoimmune or inflammatory processes. Clinicians can select the most appropriate treatment option based on individual patient conditions. Therefore, precise localization and evaluation of the stenosis are essential to ensure safe and effective treatment. This review summarizes current research on TS diagnosis and assessment, encompassing functional, imaging, and bronchoscopy methods. The characteristics, advantages, and disadvantages of each technique are discussed in relation to their application in the diagnosis and assessment of TS. Bronchoscopy is considered the cornerstone of TS diagnosis, and novel adjunct imaging modalities have emerged to enhance its accuracy. We explore advanced endomicroscopic methods, such as endobronchial ultrasound (EBUS), photoacoustic endoscopy (PAE), optical coherence tomography (OCT), and confocal laser endomicroscopy (CLE). Among these, EBUS is clinically approved for diagnosing lesions with high resolution and acceptable penetration depth. OCT and CLE offer real-time imaging for peripheral lesions and potentially malignant nodules, but their use is limited by cost and availability in low-resource settings. Therefore, bronchoscopy, with biopsy techniques as needed, remains the optimal approach for diagnosing tracheal stenosis.

Keywords: Tracheal stenosis, Endobronchial ultrasonography, Optical coherence tomography, Confocal laser endomicroscopy, Advanced airway imaging, Photoacoustic endoscopy

Background

Tracheal stenosis (TS) is characterized by a progressive narrowing of the trachea due to various etiological mechanisms, primarily linked to inflammatory reactions. Benign TS can result from prolonged intubation or tracheostomy, anastomotic strictures, intrinsic or extrinsic airway tumors, inflammatory or infectious processes, and foreign bodies. Malignant TS may arise from adjacent malignancies (such as mediastinal, lung, and thyroid cancers), primary airway tumors (including squamous cell carcinoma, carcinoid tumor, mucoepidermoid carcinoma, and adenoid cystic carcinoma), and metastatic tumors (e.g., renal cell carcinoma, breast cancer, melanoma, colorectal cancer) [1]. Etiopathogenesis studies indicate that prolonged intubation is the most common cause of

TS development [2]. Symptoms vary depending on the severity of the stenosis and the patient's cardiorespiratory reserve. While some patients remain asymptomatic, others may experience dyspnea, wheezing, stridor, or respiratory failure [3].

The primary criterion for diagnosing TS is a reduction in the cross-sectional area (CSA) of the airway lumen by more than 50% [4]. Several classification systems exist for grading stenosis based on the affected site: Bogdasarian for posterior glottis stenosis, Cohen's grading for anterior glottic stenosis, and Myer-Cotton for subglottic stenosis [5]. Bronchoscopy is commonly used to assess stenosis by measuring the percentage of lumen obstruction [6]. Beyond diagnosing TS, it is essential to evaluate the cause, etiology, extent of malignancy, and structural changes to understand their impact on the patient's functional impairments and inform better management [7].

Different approaches for diagnosing and assessing TS offer varying advantages and disadvantages in terms of invasiveness, applicability to all patients, and the ability to detect stenosis site, severity, morphology, and pathology. A comprehensive review of the latest diagnostic techniques can help pulmonologists choose the most appropriate method based on their specific needs, accuracy, and available technologies. This review summarizes current approaches for preoperative TS evaluation, including diagnostic and assessment techniques, along with their advantages and limitations.

Recent advanced bronchoscopic techniques for assessing peripheral airway obstruction fall outside the scope of this review and can be studied elsewhere [8, 9].

Diagnostic methods

Pulmonary function tests (PFT)

The first step of TS diagnosis is history and physical assessments. They include reports on stridor during or at rest, exercise, physical activity, voice evaluation, and lung function tests mostly applicable in the adult population (e.g., spirometry, body plethysmography, impulse oscillometry) [10]. Figure 1 illustrates spirometry results comparing normal function with fixed upper airway obstruction, where obstruction leads to symmetric flow reductions on both limbs of the flow-volume loop during inspiration and expiration. The obstruction causes symmetric flow reductions on both limbs of the flow-volume loop during inspiration and expiration. Four parameters are usually used to diagnose patients with fixed upper airway obstruction: (1) the ratio of forced expiratory volume in 1 s (FEV1) to peak expiratory flow, which should be greater than 10 mL/L/min; (2) the ratio of maximal expiratory flow at 50% of vital capacity (FEF50) to maximal inspiratory flow at 50% of vital capacity (FIF50), which should be greater than 1; (3) FIF50, which should be less than 100 L/min; and (4) the ratio of FEV1 to forced expiratory volume in 0.5 s (FEV0.5), which should be greater than 1.5 [11]. However, the correlation between spirometric values and the severity of subglottic stenosis is often poor. The discrepancies between spirometry results and endoscopic findings may arise from variations in patient cooperation during tests. Moreover, functional spirometry outcomes can differ between patients with the same anatomical degree of obstruction due to variations in intra-luminal airway pressure and lung capacities [12]. Researchers found correlations between plethysmography parameters and rigid bronchoscopy results in cases with post-intubation tracheal stenosis [13]. Verbanck et al. found that the forced oscillation test measures the severity of the tracheal stenosis (flow dependence of resistance), which is

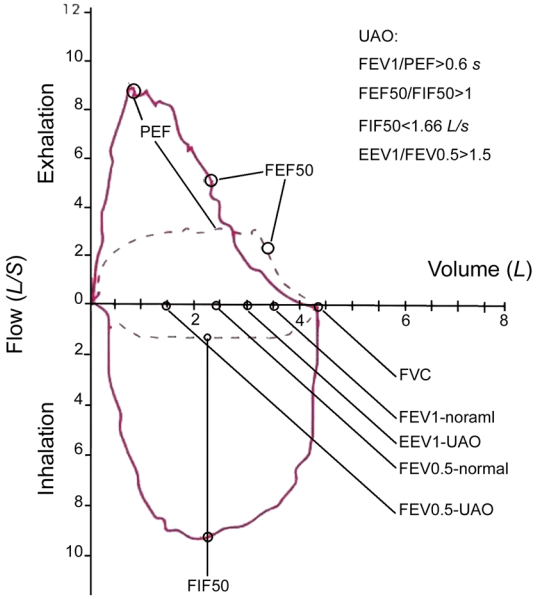

Fig. 1 Solid line is the normal flow–volume loop compared to the dashed line loop which is consistent with a fixed upper airway obstruction (UAO)

not disturbed by the presence of concomitant peripheral obstructions [14]. In addition, a study by Linhas et al. linked reactance at 5 Hz to tracheal stenosis, noting a decrease in reactance with increasing TS severity, although no significant correlation was established between resistance and stenosis severity [15]. While these assessments provide valuable information, they do not specify the exact location, morphology, or typology of airway stenosis, necessitating further imaging for complete evaluation.

Computed tomography (CT)

CT is obligatory for cases with Cotton-Myer stenosis grade of 3 or 4 without the urgent need for tracheotomy. Helical CT offers advantages over axial CT in detecting subtle airway stenosis, obliquely oriented airways, the disease craniocaudal extent, and differentiation with adjacent mediastinal structures. However, CT diagnosis of tracheal stenosis can be influenced by patient movements and secretions [16]. In addition, the risk of radiation exposure makes CT unsuitable for repeated use, particularly in young patients [17]. Recent advancements in higher resolution CT (HRCT) allow for faster and more accurate measurement of airway lumen. Advanced image-based quantification techniques, such as multidetector-row spiral computed tomography (MDCT), provide quicker data acquisition than bronchoscopy. Post-processing techniques, including volume rendering, multiplanar reformation, and virtual bronchoscopy, can be applied using MDCT. Among these, virtual endoscopy is the most effective CT method for comprehensive visualization of tracheal stenosis due to its sensitivity, specificity, and accuracy [18].

Magnetic resonance imaging (MRI)

The main disadvantage of CT scans is radiation exposure, which increases the risk of future malignancy—unlike MRI, which has no such risk. MRI is seldom used for

visualizing lung airways due to weak signal strengths from pulmonary tissues. However, recent advancements in ultrashort echo time have improved the structural imaging of the lungs [19, 20]. Studies show that airway diameters measured by this new MRI technique correlate with bronchoscopic measurements in patients with bronchial stenosis associated with lung transplantation [21]. Nonetheless, no radiological methods can adequately evaluate the mucosal surface.

While MRI is a powerful diagnostic tool, its effectiveness for assessing tracheal stenosis is limited. The long acquisition times of MRI scans can pose challenges, particularly for patients who may struggle to tolerate lengthy procedures, such as those with dyspnea. This extended duration can lead to motion and breathing artifacts. In addition, MRI results can be influenced by the respiratory cycle, secretions, and variability among observers, making it unsuitable for patients who cannot perform end-inspiration breath-holding maneuvers [16]. Furthermore, the large size of MRI machines complicates their use in intensive care units.

Ultrasound (US)

US is a swift, portable, and widely accessible technique that can be routinely performed in the ICU [22]. Point-of-care ultrasound of the upper airway serves as a primary non-invasive tool for airway management, including confirming tracheal intubation, tracheostomy placement, and assessing tracheal diameter [23]. The subglottic transverse diameter measured using ultrasound is related to the outer diameter of the endotracheal tube [24]. US was well correlated with videobronchoscopy and endotracheal tube sizing in pediatric patients. It is effective in noninvasively monitoring changes in subglottic lesions but often underestimates the absolute lumen diameter and can only measure transverse cervical tracheal diameter [25]. US can also predict TS in children with mucopolysaccharidosis [26]. Research by El-Naga et al. demonstrated a strong correlation between laryngeal US and CT measurements [18]. Lakhal et al. discovered a significant association between subglottic diameter assessed via US and MRI [27]. El-Anwar et al. compared the length, diameter, and nature of subglottic stenosis diagnosed by US and CT and concluded that the superficial US is a reliable diagnostic imaging tool [28]. While many researchers evaluated the diagnostic capability of US for upper obstructions, it should be noted that US is an adjunct tool for diagnosing post-intubation tracheal stenosis. Its sensitivity is comparable to that of fiber optic bronchoscopy, but its specificity is lower [29].

Photoacoustic tomography (PAT)/multispectral optoacoustic tomography (MSOT)

PAT is an imaging modality that combines optical excitation and acoustic detection. It offers a spatial resolution of 150 μm and a depth penetration of 25 mm. The inter-observer reproducibility for measuring wall thickness and cross-sectional area is high. However, PAT cannot visualize smaller airways due to the large size of the PAT probe. MSOT is similar to PAT but distinguishes absorbers based on their spectral signatures due to either endogenous materials or exogenous contrast agents [30]. MSOT has been evaluated for imaging in a rabbit tracheal stenosis model [31]. It can also analyze deoxygenated and oxygenated hemoglobin, as well as collagen content. While PAT and MSOT

have clinical applications in imaging thyroid, breast, skin, extremities, large blood vessels, and lymph nodes, they have yet to be implemented clinically for evaluating TS.

Endoscopy

TS is an urgent medical condition that requires prompt management, but surgical intervention is rarely employed [32]. The primary diagnostic and interventional approach for TS is airway endoscopy, which addresses both benign and malignant airway stenosis as well as tracheomalacia. This procedure uses a bronchoscope and a light source to illuminate the airways. Both rigid and flexible bronchoscopies are valuable for diagnosing and treating TS. Flexible bronchoscopy is well-tolerated and often requires only mild sedation, while rigid bronchoscopy typically necessitates general anesthesia. Rigid bronchoscopy provides excellent visualization and can accommodate additional instruments within its working channel. It also allows for airway stabilization and effective tamponade to control bleeding in central vascular lesions, which are not accessible with flexible scopes [33]. The advantage of flexible bronchoscopy is its capacity for repeated maneuvers (e.g., tidal breathing, forced dynamic maneuvers, and coughing). However, it has limitations, including an inability to provide accurate measurements of airway caliber due to optical distortion and respiratory motion. Bronchoscopy demonstrates a favorable level of intra- and inter-observer agreement, regardless of the practitioners' training and experience [34]. Nevertheless, human quantification of airway stenosis from bronchoscopy images can significantly differ from CT measurements. Banach et al. proposed a computer-based airway stenosis quantification, which offers smaller error margins compared to human assessments [35].

Bronchoscopy image analysis can either underestimate or overestimate the degree of tracheal stenosis (TS). A more accurate estimation can be achieved by analyzing bronchoscopy videos [36]. However, this is not a real-time procedure and requires a post-operative time [37]. The developed software named SENSA can compute the degree of TS from cross-section area contours automatically extracted from video frames in less than 10 s [38]. The limitation of this method is that the distance of the scope tip from the stenosis location during bronchoscopy recording and frame selection affects the results, and a calibration method is needed for the measurement of actual CSA [39]. Although the severity of stenosis could be measured precisely during bronchoscopy, the airway wall structure could not be visualized. So, bronchoscopic assessment usually utilizes the transbronchial needle aspiration technique to sample lesions for histology specimens.

Advanced endoscopic optical imaging

The development of new real-time optical imaging techniques during bronchoscopy is crucial. Optical imaging is preferred due to its use of low-intensity and non-ionizing radiation, which allows for extended exposure times. However, increased endoscopic diameter and the cost of advanced technology are disadvantages [40]. Despite these challenges, recent advances in microfabrication and optical methods have enabled high-resolution visualization of small airways.

Pepper et al. developed an endoscopic airway measurement (EAM) method using an endoscope, an optical instrument, and post-processing software [41]. This technique overcomes limitations related to endotracheal tube approximation, especially in

non-circular stenoses or airways with distal or multilevel lesions. A calibration image is obtained by placing a ruler at the optical instrument end. Then the optical instrument tip is aligned with the area of interest to capture an endoscopic image. Both the endoscopic and calibration images are processed to compute airway dimensions. Measurements of simulated tracheas using EAM differed by approximately 0.7 mm from direct measurements on large animal models (Ovis aries). The mean percent difference in diameter between EAM and 3D fluoroscopic reconstruction, and their evaluation of resected tracheas was 4.98% and 10.74%, respectively. These differences are not considered significant, and this technique is readily accessible without additional costs.

A novel stereovision fiber optic bronchoscope has been developed, featuring two independent lenses at the device tip [42]. This stereoscopic assessment uses triangulation to calculate object coordinates from the endoscope's distal end. Airway sizes measured with this method correlate well with those obtained using HRCT-based virtual bronchoscopy.

Stereovision bronchoscopy offers an advantage over HRCT-based virtual bronchoscopy by discerning the color of the airway mucosa, which is crucial for identifying lesions like inflammation and tumors. Nobuyama et al. compared airway measurements for tracheobronchial stenosis using stereoscopic bronchoscopy and MDCT [43]. They reported a maximum bias of 1.2 mm in diameter measurements, indicating that stereoscopic endoscopy holds promise for precisely evaluating airway diameter during interventions such as stent sizing and choke point measurements, compared to MDCT. The superiority of this method over MDCT stems from its direct line-of-sight approach and its applicability to patients with severe stenosis who cannot breath-hold effectively. In addition, stereovision measurements can be repeated during interventions to account for varying degrees of stenosis during breathing. Stereoscopic bronchoscopy is also useful for assessing airway improvements after procedures like laser ablation and balloon dilation.

Assessment techniques

Advanced imaging techniques with near-microscopic resolution could aid in visualizing hypertrophic tissue thickness and cartilage structure, guiding optimal TS management. Moreover, these modalities enable the detection of paratracheal tumors invading the trachea and measurement of wall invasion depth. Endobronchial ultrasonography (EBUS) is currently the only clinically approved high-resolution tool for microstructures. Other advanced endoscopic optical imaging techniques such as photoacoustic endoscopy (PAE), autofluorescence imaging, narrow-band imaging, confocal laser endomicroscopy (CLE), optical coherence tomography (OCT), and laser Raman spectroscopy have been devised for high-resolution in vivo imaging at the cellular and subcellular levels in disease state, as comprehensively reviewed by Ohtani et al. [44], and He et al. [45]. OCT and CLE have recently made strides in their application to pulmonary diseases, presenting promising prospects for the future. However, they have not yet been clinically implemented [46, 47].

Figure 2 compares the spatial resolution and penetration depth of several imaging techniques that are promising for diagnosing and assessing the causes of TS. In airway imaging, the trade-off between resolution and penetration depth is critical when

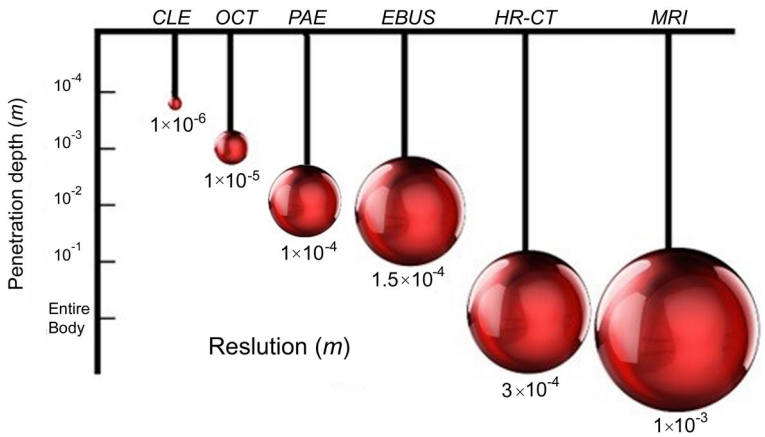

Fig. 2 Spatial resolution (circles) and penetration depth (Y-axis) of presented imaging techniques [48]

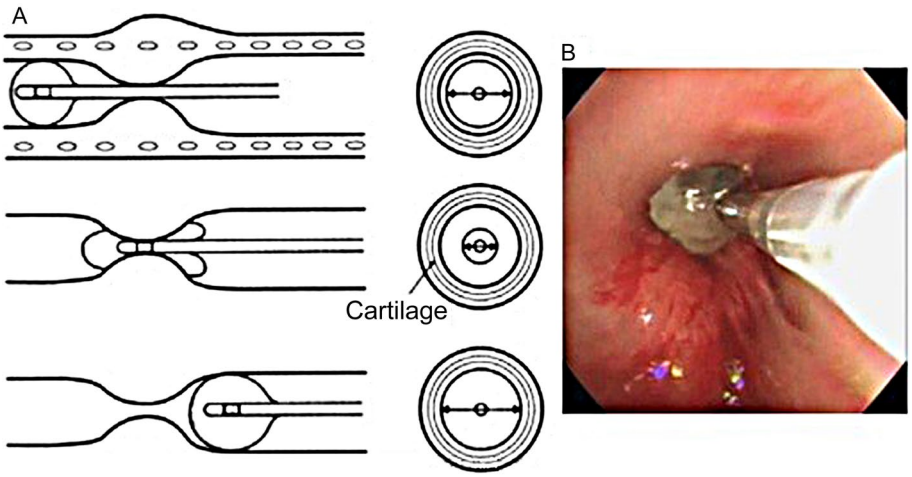

Fig. 3 **A** A schematic of the EBUS procedure. **B** The dilated balloon in contact with the stenotic site of the airway during bronchoscopy; reprinted with permission from [53]

choosing an imaging modality. Higher resolution provides detailed images of intricate anatomical features but often limits penetration depth. Conversely, greater penetration depth allows for examining deeper structures but typically reduces resolution. For example, optical coherence tomography offers cellular-level resolution but has a penetration depth of only a few hundred micrometers. Therefore, as image resolution improves from MRI to CLE, a more detailed view of the airway wall is achievable.

Endobronchial ultrasonography (EBUS)

EBUS is a safe and well-tolerated technique that has evolved over the past decade. It utilizes a balloon-sheathed radial probe inserted through the bronchoscope's working channel to detect stenotic sites in the airway. The balloon, inflated with saline, contacts the airway wall, providing a comprehensive view of its circumference (Fig. 3). This imaging reveals the airway's layered structure and any tumor invasion. The stenosis length can be measured by moving the balloon from the distal to the proximal end of the lesion. This promising approach has demonstrated a strong correlation with bronchoscopy

images for measuring central obstructions, offering more objective and reproducible measurement than visual estimates [49, 50]. In addition, EBUS provides more accurate depth measurements of tumor invasion compared to bronchoscopy or HR-CT [51]. Radial EBUS has evolved through its integration with transbronchial needle aspiration (TBNA) techniques, enhancing the diagnostic yield for peripheral pulmonary lesions [52]. While it is somewhat overshadowed by convex probe-EBUS in certain applications, radial EBUS remains crucial for bronchoscopic evaluation of lung nodules, especially those located peripherally.

Photoacoustic endoscopy (PAE)

The imaging process of PAE is illustrated in Fig. 4. A pulsed laser excites the photoacoustic (PA) signal by emitting a focused beam into the imaging probe through a condenser lens, stimulating the target tissue. A US transducer detects the resulting PA signal, enabling simultaneous US imaging. To differentiate between PA and US signals, a delay unit could be used to delay US pulse emission by a few nanoseconds. For radial scanning, a scanner equipped with an optical rotary joint and slip ring can transmit optical and electrical signals across rotating interfaces, allowing for a miniaturized imaging probe. PAE has been adapted to the photoacoustic effect similar to PAT. Like EBUS, PAE requires direct contact of the probe with the airway wall. This technique has been tested on animal tissue in preclinical trials [54–57]. Advances in PAE systems and representative probe configurations for different preclinical applications are reviewed by Li et al. [58]. Besides, dual and multimodal PAEs including photoacoustic-ultrasound, photoacoustic-optical and photoacoustic-ultrasound-optical endoscopy have been developed [59].

The most research application of PAE is in intravascular, esophageal, gastrointestinal, and urogenital imaging.

One of the significant challenges in using PAE for lung imaging is the attenuation of acoustic signals caused by air in the alveoli and the complex structure of lung tissues. This results in difficulties in obtaining clear images of internal lung structures, as current methods can only discern the outer contours of the lungs without specific details. Respiratory motion can also introduce significant artifacts during endoscopic procedures, degrading image quality. Future research should focus on integrating various filtering algorithms for artifact removal at appropriate processing stages [60, 61]. Moreover, the clinical translation of PA is impeded by the lack of laser sources capable of delivering the necessary pulse energy and repetition rates. An ideal laser would have high repetition

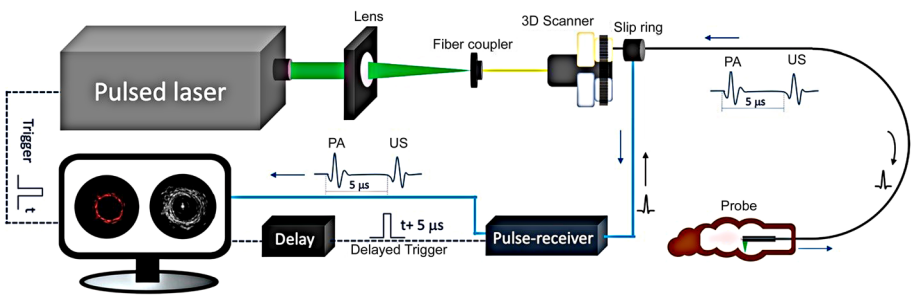

Fig. 4 Photoacoustic imaging process [58]

rates, maintain high pulse energy, allow rapid wavelength sweeps, a wide sweep range, and be compact for practical use [58]. Despite notable advancements, the majority of the work is still in the preclinical phase, necessitating further efforts to accelerate clinical translation [62]. Therefore, clinical approval is necessary before PAE can be incorporated into endoscopic optical imaging of the airway wall.

Optical coherence tomography (OCT)

In OCT, two identical beams are emitted from a low-coherence broadband light source: one beam goes to a mirror, and the other to the tissue. The interference between the back reflection or scattering signal from the tissue and the signal from the mirror is analyzed to create an image, as shown in Fig. 5 [45]. OCT provides a resolution of 10–15 μm and a depth of 2–3 mm, with minimal risk from weak near-infrared light sources.

The spatial resolution of OCT is an order of magnitude higher than EBUS, although it has a shallower depth penetration of 2–3 mm. Unlike EBUS, OCT does not require contact between the instrument and tissue or liquid coupling medium. Furthermore, OCT can capture focused images of the airway anywhere within 0–25 mm from the probe head without distortion from airway morphology or the probe position [64].

There are two main implementations of OCT: time-domain and Fourier-domain OCT. Time-domain OCT uses a moving mirror to measure depth, while Fourier-domain OCT captures all depth information simultaneously through spectral detection methods, such as spectral-domain OCT and swept source OCT. This is done by recording the interference spectrum with a spectrometer or a rapidly swept laser source.

With its high resolution and speed, Fourier-domain OCT is well-suited for detailed examinations of microstructures within tissues. Fourier-domain OCT is particularly advantageous for dynamic imaging in airway management due to its higher speed, better signal quality, and reduced motion artifacts. Its most promising application in lung diseases is distinguishing premalignant and malignant lesions from normal tissue. OCT can aid in transbronchial needle aspiration biopsy and evaluate sample quality in real-time [65].

OCT can be performed on conscious patients, reducing the risks of anesthesia and mechanical ventilation. It is a minimally invasive, non-contact imaging modality and a promising bronchoscopic diagnostic tool, especially for imaging neonatal subglottic stenosis without radiation exposure.

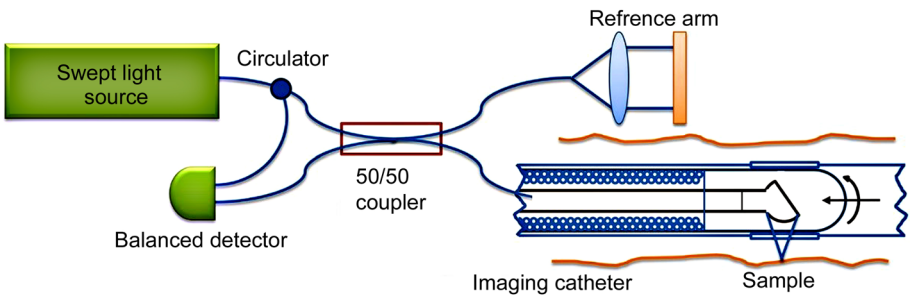

Fig. 5 Schematic diagram of the optical coherence tomography system, reprinted with permission from [63]

Endoscopic OCT probes can be classified into two types based on their scanning modes: side-imaging and forward-imaging. Side-imaging probes emit and receive scans from the side, while forward-imaging probes do so from the front. Side-viewing endoscopes are ideal for examining large areas of luminal organs, whereas forward-viewing endoscopes are better suited for ophthalmic imaging or guiding biopsies. In addition, OCT probes can be categorized as proximal-end or distal-end scanning probes, depending on the beam scanning device's location. Proximal-scanning probes are more economical, while distal-scanning probes offer faster scanning speeds and reduce refractive index variations, minimizing OCT signal distortion. Recent advances in OCT endoscopes have been thoroughly reviewed by Gora et al. [66].

Endoscopic OCT can be performed during flexible bronchoscopy by inserting a probe inside a guide sheath through the working channel of the bronchoscope [67]. Rotational scanning of the OCT probe allows for high-resolution reconstruction of the lumen cross-sectional area. The image acquisition process of endoscopic OCT is illustrated in Fig. 6 [68]. Rotational scanning in endoscopic OCT imaging can be achieved either through proximal or distal design. In proximal designs, the entire probe body rotates via an external motor, while distal designs use a single rotational element at the probe tip.

Real-time processing in OCT requires advanced computational resources, such as high-performance CPUs or GPUs, to efficiently handle intensive image processing tasks [69, 70]. Distal design schemes enhance stability for high-speed imaging of large lumen diameters, like in the airway, by preventing full constriction of the probe body by the lumen wall, which reduces vibrational motion during scanning [71].

Kwon et al. combined a 1300-nm OCT system with a servo motor for 360° imaging of an ex vivo rabbit trachea. The OCT images provided valuable information about the lumen area, stenosis shape, and submucosal and mucosal structures of the trachea, aiding in the detection of airway stenosis [72]. Its accuracy was validated by comparing OCT measurements to CT results.

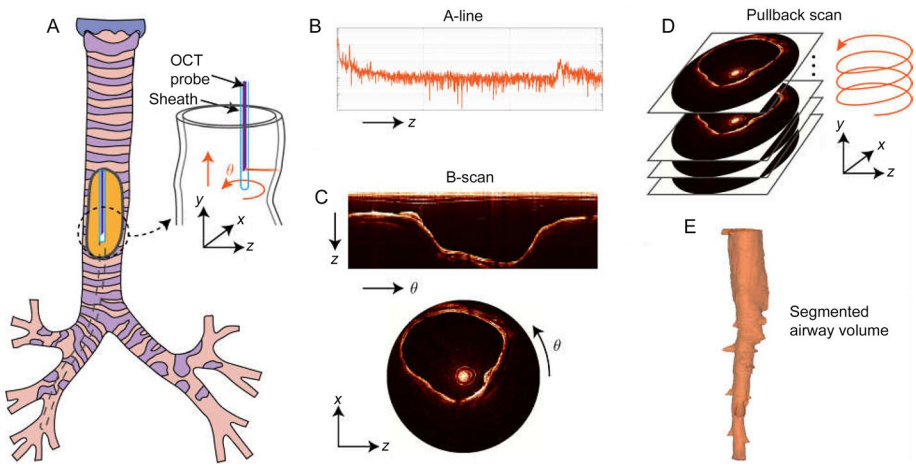

Fig. 6 Imaging process in endoscopic OCT: **a** OCT catheter in the airway, **b** output signal at one rotation angle, **c** output signals as a polar (top) or Cartesian image (bottom) representation, **d** stack of scans acquired during a pullback helical scan, **e** volumetric reconstruction of the airway derived from the pullback OCT image stack [68]

In a canine study on post-intubation tracheal stenosis, canines were intubated for 24 h before extubation and monitored for stenosis development for up to 12 days [73]. The anterolateral and bilateral airway walls were scanned using automated rotating and auto-pullback functions with a 2.5 mm OCT probe. The OCT measurements of tracheal wall thickness and grayscale values correlated with histological findings, and assessing cartilage damage helped illuminate the development of post-intubation TS.

Anatomical OCT (aOCT), a long-range scanning implementation of conventional OCT, is a new light-based imaging instrument with an imaging range of up to 30 mm, enabling visualization of large hollow organs such as the upper airway. This system uses a wavelength-sweeping vertical cavity surface-emitting laser for high-speed imaging at 200 frames per second, enabling detailed 3D anatomical modeling of the airway essential for understanding airflow dynamics and identifying obstructions. aOCT can accurately measure the lumen area and diameter of the central airways during bronchoscopy [74]. Sharma et al. propose using aOCT for intraoperatively imaging the trachea and subglottis during suspension microlaryngoscopy, both before and after endoscopic treatment of subglottic stenosis [75]. The effectiveness and safety of intra-operative aOCT imaging of the pediatric upper airway [76, 77], the intubated neonatal airway [78], and the pharyngeal airway in awake adults [79–81] and children [82] have been previously described. Figure 7 shows an OCT image of a pediatric trachea.

However, data analysis in aOCT can be challenging and time-consuming. To address this issue, Kozlowski et al. proposed a tissue segmentation algorithm for aOCT image analysis on tissue layers, which is over eight times faster [83]. In this way, a fully automatic framework to reconstruct the 3D upper airway model is presented based on aOCT imaging system equipped with a magnetic tracker [84].

The combination of OCT and EBUS was studied for imaging airway wall structure during laser-assisted treatment of laryngotracheal stenosis in two patients with post-intubation TS [85]. Both imaging techniques were performed before and after laser-assisted mechanical dilation, and again 2 weeks later. EBUS revealed thick hypertrophic tissue before treatment and thinner residual tissue 2 weeks post-treatment. OCT showed a loss of layered structure before treatment and focal high-intensity areas due to inflammation.

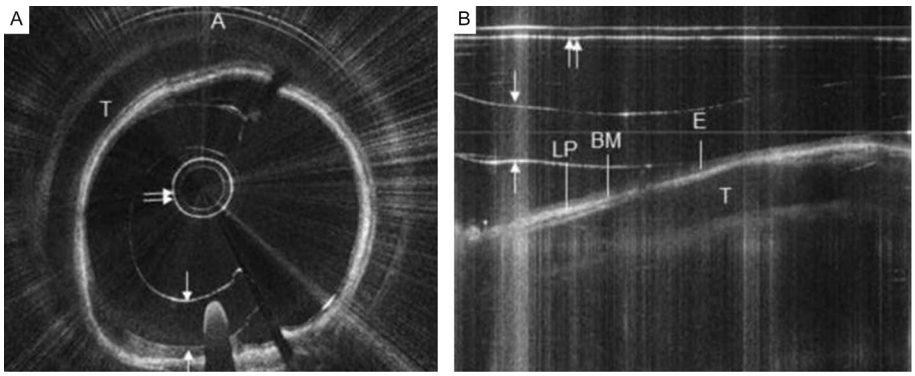

Fig. 7 OCT image of pediatric trachea, represented in polar coordinates (**A**) and cropped segment of Cartesian coordinates (**B**). A = anterior, T = tracheal cartilage, E = epithelium, BM = basement membrane, LP = lamina propria; double arrow = probe sheath, single arrows = endotracheal tube inner/outer wall. Bar = 500 µm, reprinted with permission from [76]

EBUS and OCT provide advantages over bronchoscopy by detecting hypertrophic tissue and assessing cartilage proximity at the stricture level, which may help predict stricture recurrence and reduce the need for repeated bronchoscopic interventions. The combination of OCT and PAE can enhance image contrast, spatial resolution, and penetration depth [86].

Recently, automated surface recognition and segmentation software has been developed based on OCT images. For instance, Zhou et al. develop a convolutional neural network-based OCT image analysis algorithm for automatical segmentation of airway morphology [87]. Another deep learning-based OCT image processing framework has been developed to enhance spatial resolution and signal-to-noise ratio [88]. However, challenges in using artificial intelligence in OCT imaging include variability across devices, the three-dimensional nature of the data, limited datasets, and inconsistent reporting metrics [89]. Improving data quality, utilizing multiple data sources, and enhancing interpretability are essential for successful clinical implementation.

In the future, to enhance image quality and streamline data analysis, it is crucial to implement a standardized probe fabrication protocol [76]. Standardizing imaging and post-processing protocols can reduce discrepancies among different OCT devices. While OCT offers significant advantages for diagnosing peripheral lesions, its contribution to diagnosing TS does not notably improve accuracy compared to established methods. In addition, the high cost of OCT and its reliance on manual interpretation limit accessibility in low-resource settings.

Confocal laser endomicroscopy (CLE)

CLE is an advanced real-time imaging technique with a resolution of up to 3.5 μm and a maximum depth of 50 μm. A fiber optic probe was inserted into the working channel of the bronchoscope, using laser light to illuminate the tissue and reflect back through a pinhole. This imaging technique is based on the autofluorescence properties of elastin fibers and cellular components [90]. For autofluorescence microimaging, 488 nm excitation is used, while 660 nm is applied for epithelial cell imaging with a contrast agent such as methylene blue [44]. Then 3D images of the airway wall can be reconstructed by moving the laser beam horizontally and vertically (as shown in Fig. 8). CLE is ideal for real-time imaging of the alveoli, airways, lung tumors, pleura, and lymph nodes. The terms "Needle-based CLE" and "probe-based CLE" refer to whether CLE probe advances to the tissue with or without a needle. To the best of our knowledge, there is no study about CLE in the context of TS diagnosis. However, its feasibility for laryngectomy of larynx squamous cell carcinoma patients [91] and differentiating primary flat lesions of the larynx [92] has been evaluated. Various human clinical trials using CLE are available for evaluating different pulmonary diseases [93]. It excels at visualizing cellular structures in lung lesions and mediastinal lymph nodes.

CLE provides a microscopic view of the tissue at the probe tip, with a typical field of view of about 0.5–1 mm in diameter. In larger airways, its small field of view and forward-viewing orientation hinder visualization and interpretation of overall tissue architecture. This limitation makes it challenging to mitigate motion artifacts in larger airways and maintain a clear image. The diagnostic value of CLE as a complementary tool is still under evaluation. Given its high costs and the specialized training needed, its

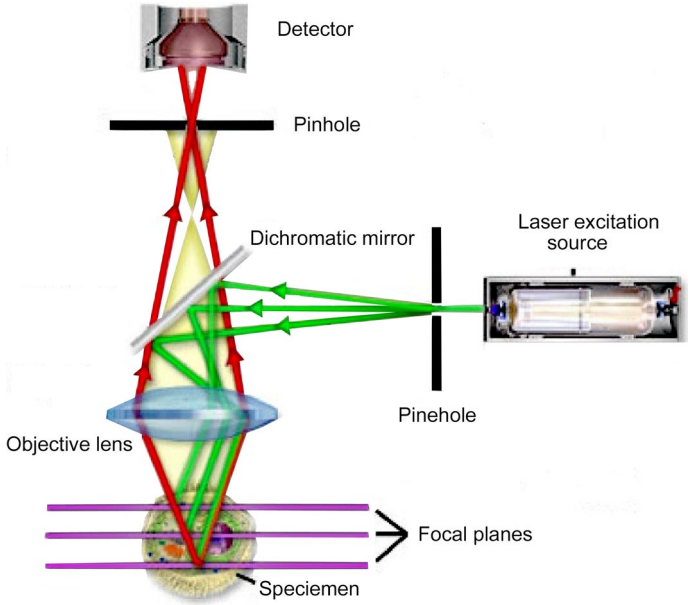

Fig. 8 Schematic of confocal laser endomicroscopy principle [94]

use may be best reserved for cases where its unique capabilities, such as detecting malignancies, can significantly improve patient outcomes, unlike in TS where alternatives like CT or conventional bronchoscopy may suffice [93].

Cost is a primary limitation for implementing CLE during bronchoscopy. In addition, manual analysis of CLE images is labor-intensive, time-consuming, and subjective. This has led to growing interest in applying artificial intelligence for automated image analysis. Moreover, the development of cost-effective modular wide-field CLE imaging systems and single-use disposable CLE fibers may increase its use in pulmonary medicine [93].

Discussion

Accurate measurement of the stenotic airway's caliber, its anatomic location, and associated morphologic features significantly influences treatment decisions. Airway caliber can be assessed through functional tests, imaging techniques, or endoscopic evaluations. The advantages and disadvantages of each method in the evaluation of TS are summarized in Table 1.

Figure 9 presents a flowchart that outlines the clinical assessment process for TS. Functional assessments provide a non-invasive estimation of airway narrowing based on the functional response rather than structural changes. However, these methods often lack reliability and may fail to pinpoint the narrowest segment of the airway contributing to flow limitation. In contrast, radiological techniques offer a more accurate assessment of airway caliber, though their effectiveness can be affected by factors such as the respiratory cycle, secretions, anatomical variations, and intra- and inter-observer variability. While CT is contraindicated for certain populations due to radiation exposure, MRI is radiation-free but impractical for patients experiencing dyspnea due to its lengthy scanning time. US may be a viable diagnostic tool for TS,

Table 1 Summarize of diagnostic methods and assessment techniques for TS

Diagnostic/ assessment technique	Advantages	Disadvantages	Key clinical applications
PFT	Swift, non-invasive estimation of obstruction presence	Limited information regarding exact location, morphology, or typology of airway stenosis	Diagnosis of normal, obstructive or restrictive pattern of lung function
CT	Comprehensive visualization of airways, including site, length and degree of stenosis	Radiation exposure risk, artifacts by respiratory movements and secretions	Imaging various body parts; specifically for lungs, visualization of airways and 3D reconstruction
MRI	Noninvasive, no risk of radiations, Comprehensive visualization of airways including site, length and degree of stenosis	Lengthy scan, breathing artifacts	Imaging various body parts of conscious patients without breathing difficulties
US	Swift, portable, non-invasive estimation of site, length and degree of stenosis	May underestimate the absolute lumen diameter, can only measure transverse cervical tracheal diameter	Abdominal, renal, cardiovascular, breast, imaging; for lung specifically, visualizing of glottic area and upper trachea
PAT/MSOT	Sub-millimeter spatial resolution with a penetration depth of several centimeters, High inter-observer reproducibility	Still in preclinical phase	Tumor, thyroid, cardiovascular, breast, skin, imaging
Endoscopy	Comprehensive visualization of airways including site, length and degree of stenosis	Invasive, may under or overestimates the degree of TS, Unable to visualize airway wall structure	Diagnosis and management of various airway and lung diseases, e.g., tracheal stenosis
EBUS	Resolution of 100 microns, penetration depth of 1 cm, Visualization of site, length and degree of stenosis, wall structure and tumor invasion into the airway wall	Invasive, needs direct contact with the airway wall	Stage lung tumors and diagnose mediastinal diseases
PAE	Functional optical contrast with high spatial resolution and maintains the benefits of EBUS	Invasive, requires direct contact with the airway wall, signal attenuation in cavity structures, still in preclinical phase	Intravascular, esophageal, gastrointestinal, and urogenital imaging
OCT	High resolution of 10 µm and depth penetration of 2–3 mm, focused image despite no contact with wall, real-time visualization of site, length and degree of stenosis and wall layers, applicable in conscious patients, suitable for imaging neonatal TS	Minimally invasive, higher cost	Retinal imaging, glaucoma detection, visualization of coronary arteries

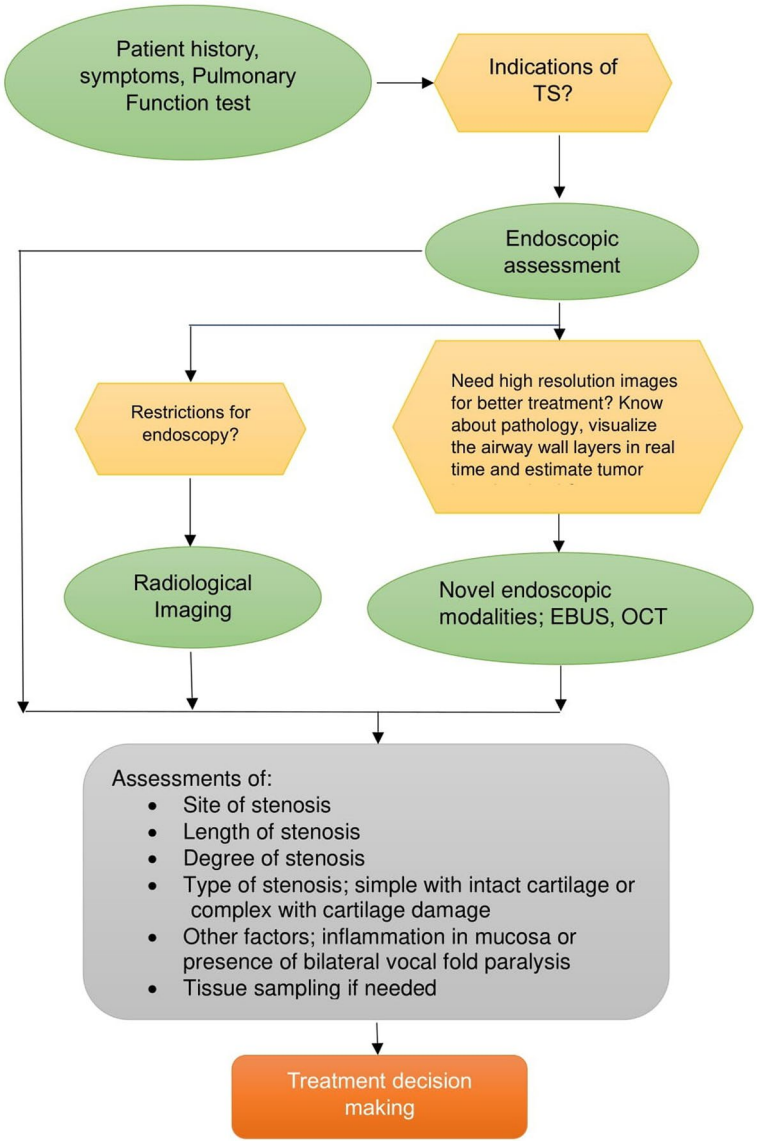

Fig. 9 Flow chart of clinical assessments of TS

showing comparable sensitivity to radiological measurements, although it tends to underestimate the lumen diameter. PAT/MSOT is an emerging non-invasive method that integrates optical imaging and acoustic analysis, yet further clinical studies are needed to assess its efficacy in lung lesion evaluation.

Bronchoscopy remains the gold standard for diagnosing TS. As the proficiency of pulmonologists in bronchoscopy improves, advanced techniques have been developed to enhance visualization accuracy. EAM and stereoscopic endoscopy provide optical imaging with resolution comparable to radiological techniques. Although these endoscopic methods effectively assess stenosis severity, innovative endomicroscopic imaging techniques are capable of visualizing micron-scale tissue structures.

However, their performance, limitations, and additional costs must be considered for routine clinical application.

Although EBUS is clinically approved and widely utilized for diagnosing and staging lung cancer, its higher costs compared to standard bronchoscopy limit its adoption in clinical practice for TS. PAE remains in the preclinical stage and faces challenges such as inadequate laser sources and acoustic signal attenuation in airway cavities. OCT provides detailed visualization of airway tissues but requires time-consuming manual interpretation and has high costs (ranging from $40,000 to $150,000), limiting access primarily to large medical centers and resource-rich environments.

Conclusion

Standard bronchoscopy continues to be the primary approach for diagnosing visible lesions in the lungs. However, the accuracy of this technique can be significantly improved by incorporating advanced methods such as EAM or stereovision techniques, alongside standardized image processing, calibration, and meticulous bronchoscope control. Innovative endoscopic imaging methods like EBUS, OCT, and CLE offer substantial benefits for diagnosing central and peripheral pulmonary lesions, facilitating precise biopsies. EBUS has become a valuable adjunct in clinical practice due to its minimal additional time requirements and low side effects, but it has not reached standard practice for TS diagnosis. While OCT and CLE have potential benefits for detecting neoplastic lesions, they do not significantly improve TS diagnostic accuracy compared to established techniques. Adopting these new modalities requires substantial changes to the current TS diagnosis workflow, which may not be deemed necessary by clinicians. Factors such as cost, limited availability, and lack of standardization contribute to the restricted use of OCT and CLE in routine clinical TS diagnosis.

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