

Diagnostic Value of the Maximal Expiratory Flow–Volume Curve for Central Airway Obstruction

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Objective: To investigate the factors associated with plateau-like changes during the expiratory phase of maximal expiratory flow–volume (MEFV) curves and their diagnostic value in identifying central airway obstruction (CAO).

Methods: Totally 59 patients with expiratory phase plateau-like changes in the MEFV curves who were treated in Henan Provincial People's Hospital from January 2019 to November 2020 were included in this retrospective analysis. Patients with CAO were recruited into the experimental group, and those without CAO were recruited into the control group. Peak expiratory flow (PEF), forced expiratory flow (FEF) 25% (FEF25), 50% (FEF50), 75% (FEF75), forced expiratory volume in 1 second (FEV1), and vital capacity (VC MAX) were compared between two groups. The receiver operating characteristic (ROC) curve was conducted for diagnostic value.

Results: There were 12 cases in the experimental group (8 males and 4 females) and 47 cases in the control group (15 males and 32 females). Analyses using a Chi-squared test and a normal test showed that CAO was correlated with PEF, FEF25, FEF50, FEF75, FEV1, VC MAX, and their actual/predicted values ($P < 0.05$). The area under-curve (AUC) of PEF was 0.966 (95% confidence interval [CI]: 0.912–1.000), and the AUC of actual PEF/predicted PEF (%) was 0.966 (95% CI: 0.918–1.000). The AUC of FEF25 was 0.915 (95% CI: 0.805–1.000), and 0.908 (95% CI: 0.782–1.000) of actual FEF25/predicted FEF25 (%). The ROC curves suggested that PEF, FEF25, and their actual/predicted values had a high diagnostic value for CAO.

Conclusion: This study showed that MEFV curves with expiratory phase plateau-like changes were not specific to patients with CAO; they could also be seen in patients without CAO, and they were highly indicative of CAO when combined with a significant decrease in PEF, FEF25, and their actual/predicted values. In subjects without CAO, the MEFV curve can form an expiratory phase plateau when the driving pressure is high enough and the equal pressure point and/or the choke point remains in the large airway.

Keywords: expiratory phase plateau, central airway obstruction, equal pressure point, choke point

Introduction

Central airway obstruction (CAO) is defined as the obstruction of the trachea, carina, right and left main bronchi, and intermediate segmentary bronchi.¹ According to its anatomical location and variability, CAO can be classified into variable intrathoracic airway obstruction, variable extrathoracic airway obstruction, and fixed airway obstruction. The normal trachea has an anteroposterior diameter of about 18 mm and a left and right diameter of about 23 mm. Generally, the patient has no symptoms until the inner diameter of trachea shrunk to 10 mm. Patients were often presented as dyspnea after activity, when the diameter shrunk to 8 mm, but with normal arterial oxygen partial pressure. Furthermore, the patient will have dyspnea in a calm state, complicated with localized false wheezing, dyspnea, and trismus, when the diameter is narrowed to 5 mm. The effects of any CAO will depend on several variables, including the size of the airway at the site of



the obstruction, the location of the obstruction, the nature of the lesion, and the phase of respiration. The nature of the obstruction determines whether there will be changes in severity in relation to changes in transmural pressure.²

The main medical tools for diagnosing CAO are computed tomography (CT) of the chest and bronchoscopy, neither of which are performed routinely due to the radioactive nature of CT and the invasive nature of bronchoscopy.³ Chest radiography is routinely performed for these patients but rarely provides sufficient information for diagnosis.⁴ However, pulmonary function testing is both non-invasive and convenient. Thanks to its rapid development, it is now used widely in clinical practice and is valuable for diagnosing CAO. In mild tracheal narrowing (ie $\leq 50\%$ reduction in the cross sectional area), pressure drop is similar to that which occurs through the normal glottic opening and therefore is unlikely to cause symptoms.⁵ The presence of an expiratory plateau at the end of expiration as figures indicated in the previous study,² which is characterized by a fast initial descent after the peak; this is followed by a slowly descending plateau, a second fast descending bump or knee, and finally, a slowly descending tail. Furthermore, previous study has shown that expiratory flow-volume loop test can be helpful in assessing an upper airway obstruction.⁶

In frontline clinical practice, the plateau-like change in the expiratory phase of the maximum expiratory flow-volume (MEFV) curve is often regarded as a specific indicator of CAO. This finding frequently leads to further investigations, such as radiological CT scans or even invasive bronchoscopy. However, most cases presenting with a plateau-like expiratory phase do not actually involve CAO. In addition, there are few studies exploring the causes of MEFV plateau changes, and no studies investigating the ROC curve cutoff value of CAO patients with MEFV plateau changes have been found. Herein, this study aimed to investigate the factors affecting expiratory phase plateau-like changes in MEFV curves and their sensitivity and specificity for diagnosing CAO via a retrospective analysis of subjects with expiratory phase plateau-like changes.

Patients and Methods

Patients

Totally 69 patients were diagnosed as expiratory phase plateau-like changed MEFV in Henan Provincial People's Hospital from January 2019 to December 2020. CT and bronchoscopy were the main tools to diagnose CAO. Thus, 10 patients who did not receive CT and bronchoscopy were excluded. Fifty-nine patients (23 males and 36 females aged 11–75 years with a median age of 46 years) were included in the final analysis. Twelve cases (8 males and 4 females) were complicated with CAO, and the corresponding incidence was 20.34%. There were 5 cases of endotracheal obstruction in the hilar or supratracheal lung. There was 1 case of obstruction in the following: the vocal cord and supratracheal areas, full-length obstruction in the right vocal cord with invasion of the subglottis, right vocal cord paralysis, distorted stenosis of the upper trachea, multiple chondromalacia (Figure 1), restenosis after endotracheal silicone stent implantation, and restenosis after tracheal intubation (Figures 2–4).

This study was conducted in accordance with the declaration of Helsinki and approved from the Ethics Committee of Henan Provincial People's Hospital. Written informed consent was obtained from all participants.

Methods

Data Collection

Sex, age, peak expiratory flow (PEF), forced expiratory flow (FEF) (25% [FEF25], 50% [FEF50], and 75% [FEF75]), forced expiratory volume in 1 second (FEV1), actual FEF/predicted FEF, actual FEV1/predicted FEV1, and vital capacity (VC MAX) were collected and enrolled in final analysis.

Pulmonary Function Testing

Pulmonary function testing including PEF, FEF25, FEF50, and FEF75, FEV1, actual FEF/predicted FEF, actual FEV1/predicted FEV1, and VC MAX were performed. The patients underwent FEV tests using a MasterScreen-PFT spirometer (Jaeger®, Germany) by the same pulmonary function specialist, and environmental and volume calibrations were performed before testing. The patients provided at least three flow–volume (F–V) curve checks. The curve should satisfy the following criteria: 1) without an unsatisfactory start of expiration, characterised by excessive hesitation or false start extrapolated volume or EV $>5\%$ of FVC or 0.150 L, whichever is greater; 2) without coughing during the

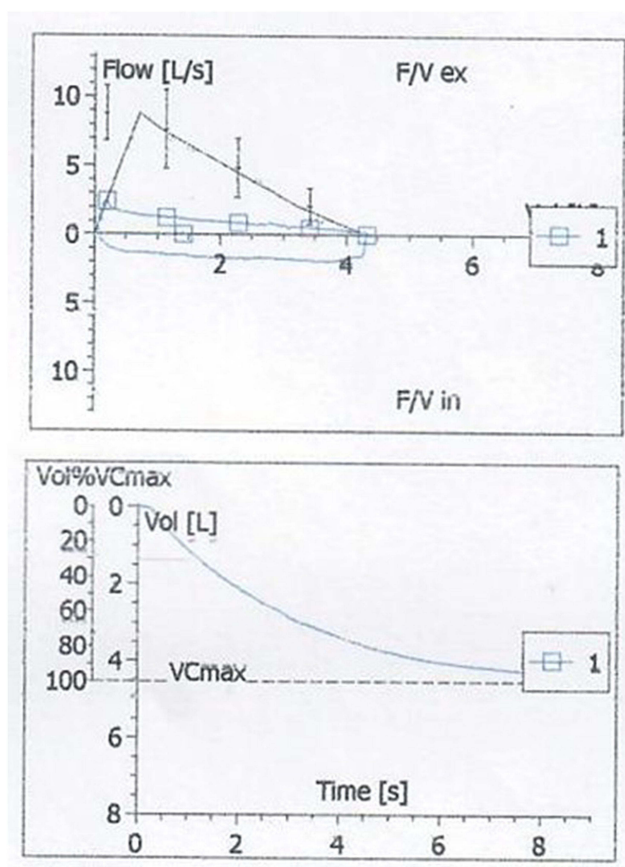


Figure 1 Chondromalacia.

first second of the manoeuvre, thereby affecting the measured FEV1 value, or any other cough that, in the technician's judgment, interferes with the measurement of accurate results; 3) without early termination of expiration (see End of test criteria section); 4) without a Valsalva manoeuvre (glottis closure) or hesitation during the manoeuvre that causes a cessation of airflow, which precludes accurate measurement of forced expiratory volume in 1 second (FEV1) or FVC; 5) without a leak; 6) without an obstructed mouthpiece (eg obstruction due to the tongue being placed in front of the mouthpiece, or teeth in front of the mouthpiece, or mouthpiece deformation due to biting); 7) without evidence of an extra breath being taken during the manoeuvre. 8) The curve was presented as burst breath, and the β angle of the initial MEFV curve was no less than 80° . The ATS/ERS quality control standards on spirometry (2005 version) was used for the inclusion of curve.² Expiratory phase plateau-like changes were observed in 59 patients, and 6 cases were complicated with inspiratory phase plateau-like changes (5 cases of obstruction in the vocal cord or vocal hilar areas and 1 case of multiple chondromalacia).

Computed Tomography Examination

A Discovery HD750 system from Georgia, USA, and a Brilliance 64- and 16-slice CT scanner from Philips, Netherlands, were used with the following parameters: a tube voltage of 120 kV, a tube current of 180 mA, a scan layer thickness of 5 mm, and a reconstruction layer thickness of 1.5 mm. The scan area included the pharynx and lungs. The CT scan of the lungs in 54 cases included 2 cases of large extrathoracic airway stenosis, 1 case of tracheal chondritis manifestation, 4 cases of large intrathoracic airway stenosis, and 47 cases of tracheal patency.

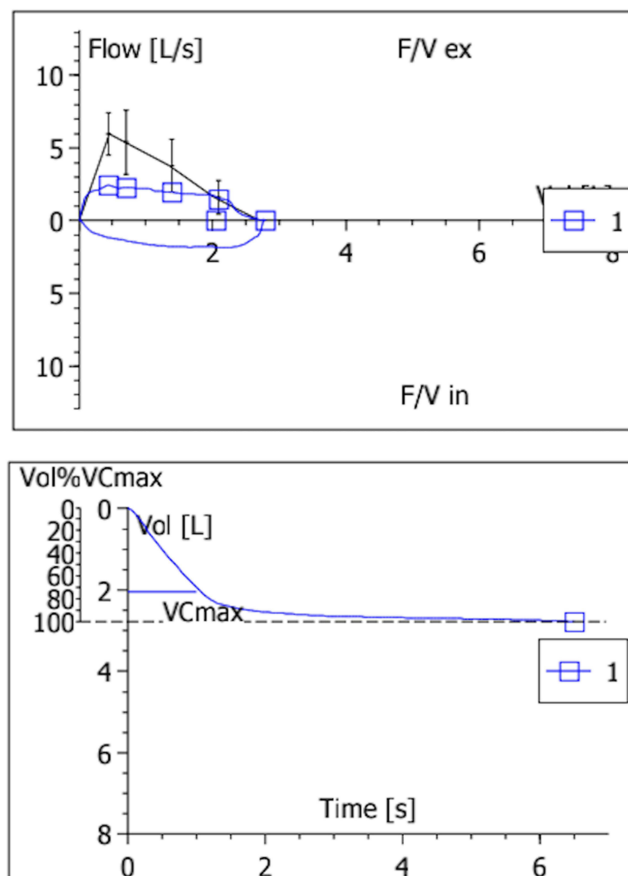


Figure 2 Post-intubation airway narrowing.

Bronchoscopy

A conventional bronchoscope (BF-240, Olympus, Japan) was used to enter the airway through a laryngeal mask to observe whether the airway was patent. This revealed two cases of large extrathoracic airway stenosis and three cases of large intrathoracic airway stenosis.

Statistical Analyses

All the data collected in this study were analyzed using SPSS 25.0 software. Normally distributed measurement data were expressed as mean \pm standard deviation (SD), while non-normally distributed measurement data were expressed as median (interquartile range), and the comparisons were examined by Student *t* test and a rank-sum test. The categorical data were expressed as *n* (%), and the differences between the two groups were examined by chi-square analysis or Fisher's exact test. The correlations from the univariate analysis were subjected to Spearman correlation analysis logistic regression analysis. Receiver operating characteristic (ROC) curves were conducted for diagnostic value for CAO. Based on the ROC curve, the cutoff values for each parameter were determined using the maximum Youden index derived from sensitivity and specificity. $P < 0.05$ was considered statistically significant.

Results

There were 8 (34.8%) male patients in the experimental group, which took significantly higher proportion than 4 (11.1%) ones of control group ($P = 0.045$). The mean age of experimental group was 55.25 ± 11.69 years old, which was significantly higher than 42.74 ± 17.80 of control one ($P = 0.025$). The body mass index was not significant different between the two groups. The PEF, FEF25, FEF50, FEF75, FEV, and their actual/predicted values in the experimental group were all significantly lower than those in the control group ($P < 0.05$) (Table 1).

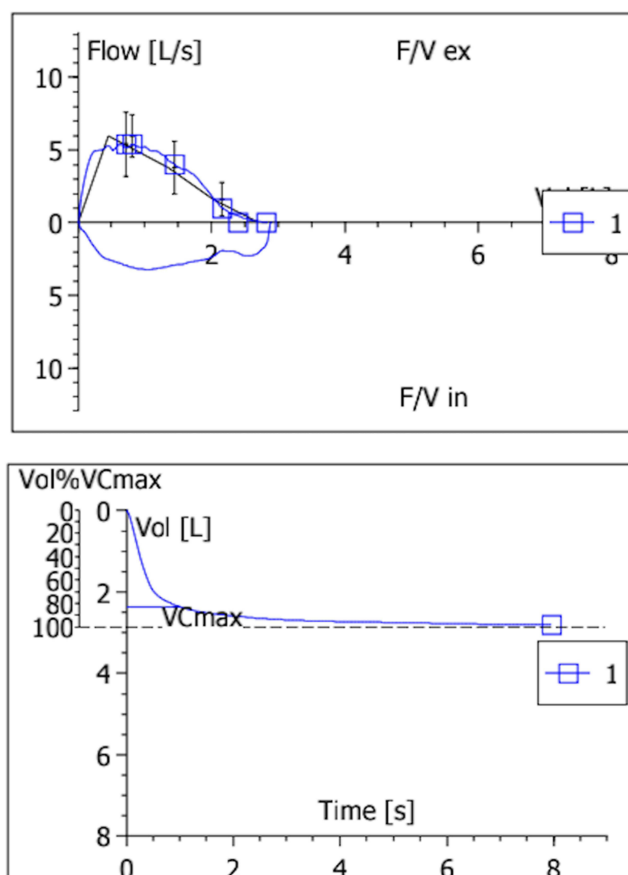


Figure 3 After balloon dilatation.

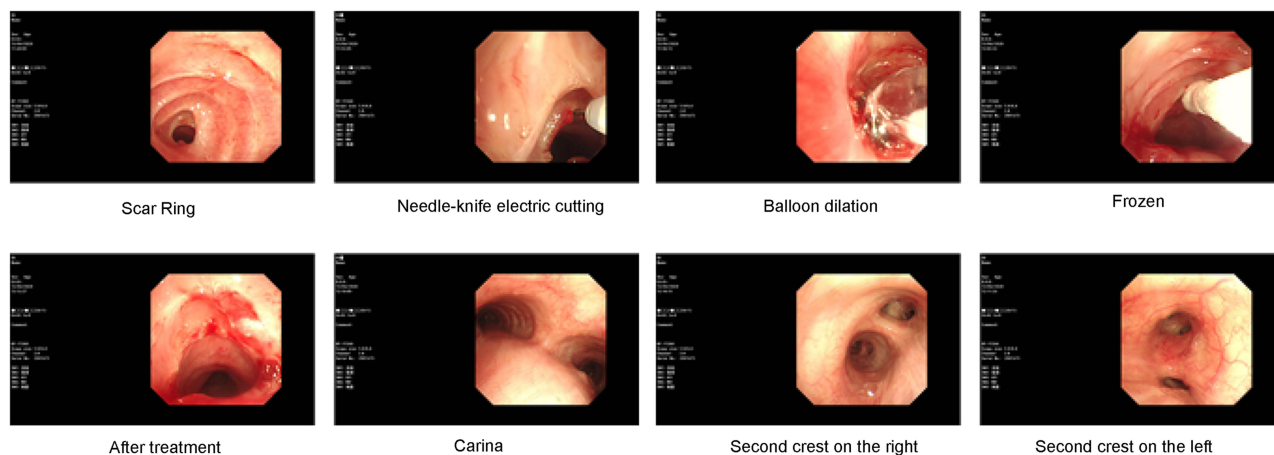


Figure 4 Electronic bronchoscopy consultation report.

The logistic regression showed that PEF, FEF25, FEF50, FEV1, and their actual/predicted values were independent risk factors for the development of CAO (Table 2). For parameters with an area under the curve (AUC) greater than 0.9, the cutoff values are presented in Table 2. The ROC curve showed (Figure 5) the area under-curve (AUC) of PEF was 0.966 (95% confidence interval [CI]: 0.912–1.000), and the AUC of actual PEF/predicted PEF (%) was 0.966 (95% CI: 0.918–1.000). The AUC of FEF25 was 0.915 (95% CI: 0.805–1.000), and 0.908 (95% CI: 0.782–1.000) of actual FEF25/

Table 1 Baseline Characters of Included Study

Variables	Experimental Group	Control Group	P-value
Sex ^a (%)			
Male	8 (66.67%)	15 (31.91%)	0.045
Female	4 (33.33%)	32 (68.09%)	
Age	55.25 ± 11.69	42.74 ± 17.80	0.025
PEF	2.87 ± 1.26	6.24 ± 1.30	<0.001
PEF (actual/predicted) (%)	40.93 ± 21.6	90.52 ± 13.96	<0.001
FEF25	2.31 ± 1.28	4.87 ± 1.34	<0.001
FEF25 (actual/predicted) (%)	37.18 ± 23.28	79.83 ± 16.41	<0.001
FEF50	1.86 ± 1.03	3.81 ± 1.13	<0.001
FEF50 (actual/predicted) (%)	46.55 ± 26.14	89.08 ± 22.55	<0.001
FEV1	1.94 ± 0.64	3.07 ± 0.77	<0.001
FEV1 (actual/predicted) (%)	70.82 ± 27.20	107.48 ± 12.49	<0.001
VC MAX (actual/predicted) (%)	99.67 ± 15.08	110.42 ± 14.15	0.024

Note: ^afisher's exact test.

Table 2 Area Under the ROC Curve

Variables	Area	SD ^a	95% CI	P-value ^b
PEF	0.966	0.028	0.912–1.000	<0.001
Actual PEF/predicted PEF (%)	0.966	0.025	0.918–1.000	<0.001
FEF25	0.915	0.056	0.805–1.000	<0.001
Actual FEF25/predicted FEF25 (%)	0.908	0.064	0.782–1.000	<0.001
FEF50	0.893	0.057	0.780–1.000	<0.001
Actual FEF50/predicted FEF50 (%)	0.881	0.059	0.766–0.997	<0.001
FEF75	0.718	0.085	0.551–0.885	0.021
FEV1	0.876	0.063	0.753–0.999	<0.001
Actual FEV1/predicted FEV1 (%)	0.883	0.076	0.735–1.000	<0.001
Actual VC MAX/predicted VC MAX (%)	0.726	0.090	0.550–0.902	0.016

Notes: There should be at least one binding value among the test result variables including actual/predicted FEF25, FEF50, FEF75, VC MAX (%) between positive actual state group and negative actual state group. Statistics may be biased. ^aBy non-parametric assumptions. ^bOriginal assumption: true area = 0.5.

Abbreviations: ROC, receiver operating characteristic; PEF, peak expiratory flow; FEF, forced expiratory flow; FEV, forced expiratory volume; SD, standard deviation; CI, confidence interval.

predicted FEF25 (%). The diagnostic cutoff points for PEF and PEF% were 3.715L/s and 63.5%, respectively, with 83.3% sensitivity, 100% specificity, and 96.6% accuracy. The diagnostic cutoff point for FEF25 was 2.84L/s, with 75% sensitivity, 100% specificity, and 94.9% accuracy. A cutoff value of 53.6% for FEF25% yielded a sensitivity of 83.3% sensitivity of 97.9%, and accuracy of 94.9%.

Discussion

With the rapid development of pulmonary function techniques, several studies have been conducted on the analysis of pulmonary function characteristics of patients with CAO.^{7–10}

There are few studies on the causes of the expiratory phase plateau of the MEFV curve and the relationship between the relevant data and CAO. The assessment of CAO comprises spirometry, bronchoscopy, and CT.^{11–14} Some studies have shown that pulmonary function measurements are useful for the diagnosis of CAO; furthermore, forced F–V curves can not only detect large airway obstruction but also differentiate between fixed and variable CAO.^{15–18} However, clinical work has found that most patients with MEFV curves with expiratory phase plateau-like changes have bronchoscopy and/or CT findings that do not support the diagnosis of CAO. There were only 12 cases complicated with CAO in this study, which

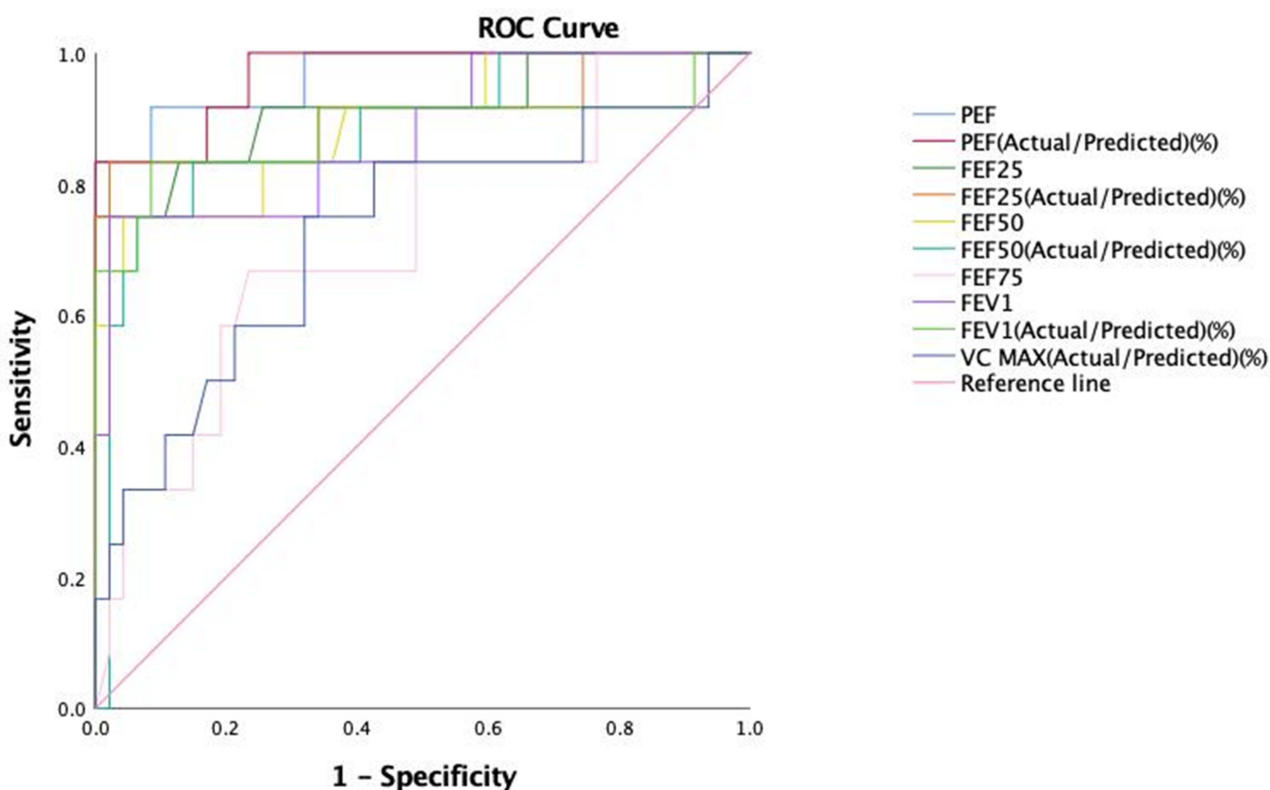


Figure 5 ROC curve.

suggesting that plateau-like changes in MEFV curves are not specific indicators for CAO. This is also consistent with some studies that have revealed a lack of specificity in lung function testing for detecting large airway obstruction.¹⁰

The shape of the MEFV curve comprises the PEF of the corresponding lung volume in which the magnitude of the flow is controlled by the flow-limiting mechanism. According to the mechanics of wave velocity theory, the shape of MEFV curves can be divided into four types: plateau, linear, convex, and concave.

There are two theories of plateau formation: the equal pressure point (EPP) theory and the choke point (CP) of the wave-speed theory of flow limitation. During forceful expiration, the pressure in the airway gradually decreases due to inertial resistance and gas viscosity as the lungs exhale along the peripheral airway to the open end. The EPP is defined as the point at which the intra-airway pressure drops to equal the intrathoracic pressure. From a kinetic perspective, the alveolar elastic retraction force is the driving force that generates flow in the airway at the alveolar isobaric point, and the resistance of the airway determines the length of the airway wall over which the alveolar elastic retraction force can effectively act to maintain patency (ie the length of the upstream segment). The greater the driving force, the lower the airway resistance and the further away the EPP becomes from the alveoli (as seen in high lung volumes during forceful expiration where the EPP moves to the large airway). As the expiratory lung volume decreases, the driving force decreases, the EPP gradually moves toward the surrounding airway, and the airway in the downstream section is squeezed by the intrathoracic pressure. As a result, the lumen becomes narrower, and the airway resistance increases, counteracting the intrathoracic pressure acting on the alveoli to increase expiratory flow, which manifests as the self-limitation of the airflow.

Compliance refers to the value of the corresponding volume change per unit pressure value change in transpulmonary pressure. The value of compliance per unit volume is the specific compliance. Transpulmonary pressure is linearly related to lung volume in the range of 0–3 kPa, and the compliance of the lung is relatively constant. Beyond this range, lung compliance changes significantly.¹⁹ Transpulmonary pressure is the driving force for flow generation. According to the above, if the transpulmonary pressure and lung tissue compliance remain relatively constant during forceful expiration, the location of the EPP and the flow rate should remain relatively constant also. The airflow's magnitude is related to the

size of the cross-sectional area of the airway, and the flow rate should be relatively constant with plateau-like changes in the F–V curve.

The wave-speed theory of flow limitation states that when a fluid flows in an elastic pipe, the maximum flow rate is limited at the CP, which is where the linear velocity of the flow equals the wave speed of the pressure-wave transmission. The maximum flow rate at the point of immediate restriction is the critical flow rate (V_c) or wave velocity flow. As it is directly proportional to the square of the specific compliance of the airway and inversely proportional to the cross section of the CP (A), which can be expressed as $V_c = 0.96A ([\delta A/\delta P] - 1/A)^{-0.5}$, CP often occurs in the part of the airway with the greatest specific compliance and the smallest cross section.²⁰ For F–V curves with plateau-like changes in the expiratory phase, the airway is first compressed dynamically, whereupon the volume is first restricted in the airway with the smallest cross section. As expiration proceeds, compression increases, and the compression segment extends to a point known as the flow-limiting segment. During the plateau, CP remains in the airway.²¹ Because of the airway's increased stiffness, the specific compliance and the change in volume caused by the pressure difference are smaller, resulting in a plateau with a slow decrease in volume. At the end of the plateau, a sudden drop in volume occurs, indicating a shift of CP from the stiffer airways to the softer bronchi. Because of the greater specific compliance of the bronchi, the same differential pressure causes a greater change in volume, resulting in a sudden drop in volume and the formation of a bump. The movement of CP is always sequential from the central to the peripheral airways, and due to the difference in specific compliance, it is inevitably reflected in the shape of the MEFV curve.¹⁰ When the compliance and driving pressure of the lung parenchyma are large and the cross-sectional area of the central airway is relatively narrow, a plateau-like change in the MEFV curve can occur.

Patients in the control group who exhibited plateau-type MEFV curves had pulmonary function indicators that were mostly within or even beyond the upper limit of the normal range, which may be related to better pulmonary compliance and higher driving pressures. In the control group, the probability of plateau-type changes was significantly greater in adult females than in adult males ($P < 0.05$), which may be related to the fact that the tracheal diameter is larger in both adult and post-pubertal males than females. Although the expiratory flow of all cases in this study had a plateau like change, the flow of the control group was large, while 12 patients (20.3%) were complicated with CAO in the experimental group (some patients with mild symptoms have not been further examined, which may lead to a higher proportion), and their high-level lung flow indicators PEF, FEF25, FEF50 and their actual to predicted ratio decreased significantly, which was consistent with previous study. Therefore, the expiratory phase plateau on MEFV curve could not be used as an independent predictor for CAO. However, it is highly valuable for CAO diagnosis, when accompanied by significant declined PEF, FEF25, FEF50 and their corresponding actual to predicted ratio.

The etiology of CAO is both complex and diverse. When airway stenosis is mild, the symptoms are not obvious, and the diagnosis is often delayed. In most patients, as the degree of airway stenosis increases, clinical symptoms increase, and dyspnea worsens and progresses rapidly, requiring close medical monitoring. The occurrence of hypercapnia and dyspnea at rest indicates the presence of fatal central airway stenosis or obstruction.¹ With the rapid development of lung function testing, many experts recognize that the MEFV curve of CAO has a specific presentation, and the expiratory phase on the F–V curve of variable intrathoracic and fixed upper-airway obstructions can show characteristic plateau-like changes. Pulmonary function testing can be used as a non-invasive indicator to monitor patients and determine if they should have interventional tests.⁷ The nature, location, and degree of obstruction can be determined initially based on MEFV curve patterns, which have important clinical significance in the early diagnosis of large airway obstructions. The present study shows that when the MEFV curve reveals an expiratory phase plateau and a significant decrease in PEF, FEF25, and their actual/predicted values, it is highly indicative of CAO.

There were also several limitations in this study. First, there were unavoidable biases due to its retrospective nature. Secondly, this was single center analysis with small sample size. Thus, all results in this manuscript should be interpreted cautiously. It should be verified by large sample prospective analysis in the future. Lastly, although our study demonstrated that MEFV curve plateau-like changes, when accompanied by significantly reduced PEF, FEF25, and FEF50 values and their predicted ratios, are highly suggestive of CAO, we were unable to further validate this relationship using interpretable machine learning methods due to the retrospective nature and limited sample size of the dataset. Future prospective studies with larger, more diverse cohorts and comprehensive

parameter collection may enable the use of advanced analytical tools, such as explainable machine learning models, to develop simplified diagnostic equations and improve the interpretability and clinical utility of these findings.

In conclusion, this study revealed that MEFV curves with expiratory phase plateau-like changes are not specific for patients with CAO since they can also be seen in patients without CAO; however, they are highly suggestive of CAO when combined with a significant decrease in PEF, FEF₂₅, and their actual/predicted values. In patients without CAO, the MEFV curve can form an expiratory phase plateau when the driving pressure is high enough and the EPP and/or the CP remains in the large airway. Pulmonary function testing can be used as a non-invasive primary screening method for patients with CAO.

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Disclosure

The authors have no conflicts of interest in this work.

References

- Li LY. Etiology and pathophysiological changes of central airway stenosis. *Zhong Hua Jie He He Hu Xi Za Zhi*. 2003;26(7):387–388.
- Stanojevic S, Kaminsky DA, Miller MR. ERS/ATS technical standard on interpretive strategies for routine lung function tests. *Eur Respir J*. 2022;60(1):2101499. doi:10.1183/13993003.01499-2021
- Murgu S, Egressy K, Laxmanan B, Doblare G, Ortiz-Comino R, Hogarth DK, Central airway obstruction: benign strictures, tracheobronchomalacia, and malignancy-related obstruction. *Chest*. 2016. doi:10.1016/j.chest.2016.02.001
- Mudambi L, Miller R, Eapen GA. Malignant central airway obstruction. *J Thorac Dis*. 2017;9(Suppl 10):S1087–S1110. doi:10.21037/jtd.2017.07.27
- Brouns M, Jayaraju ST, Lacor C, et al. Tracheal stenosis: a flow dynamics study. *J Appl Physiol*. 2007;102(3):1178–1184. doi:10.1152/jappphysiol.01063.2006
- Stanojevic S, Kaminsky DA, Miller M, et al. ERS/ATS technical standard on interpretive strategies for routine lung function tests. *Eur Respir J*. 2021. doi:10.1183/13993003.01499-2021
- Abdullah A, Arabiah A, Habib SS, et al. The Value of Spirometry in Subglottic Stenosis. *Ear Nose Throat J*. 2019;98(2):98–101. PMID: 30885002. doi:10.1177/0145561318823309
- Acres JC, Kryger MH. Clinical significance of pulmonary function tests: upper airway obstruction. *Chest*. 1981;80(2):207–211. PMID: 7249767. doi:10.1378/chest.80.2.207
- Oberg CL, Holden VK, Channick CL. Benign central airway obstruction. *Semin Respir Crit Care Med*. 2018;39(6):731–746. PMID: 30641591. doi:10.1055/s-0038-1676574
- Handa H, Huang J, Murgu SD, et al. Assessment of central airway obstruction using impulse oscillometry before and after interventional bronchoscopy. *Respir Care*. 2014;59(2):231–240. PMID: 23882104. doi:10.4187/respcare.02094
- Miller RD, Hyatt RE. Evaluation of obstructing lesions of the trachea and larynx by flow-volume loops. *Am Rev Respir Dis*. 1973;108(3):475–481. PMID: 4745245. doi:10.1164/arrd.1973.108.3.475
- Rotman HH, Liss HP, Weg JG. Diagnosis of upper airway obstruction by pulmonary function testing. *Chest*. 1975;68(6):796–799. PMID: 1192859. doi:10.1378/chest.68.6.796
- Vergnon JM, Costes F, Bayon MC, Emonot A. Efficacy of tracheal and bronchial stent placement on respiratory functional tests. *Chest*. 1995;107(3):741–746. PMID: 7533070. doi:10.1378/chest.107.3.741
- Schuermans MM, Michaud GC, Diacon AH, Bolliger CT. Use of an ultrathin bronchoscope in the assessment of central airway obstruction. *Chest*. 2003;124(2):735–739. PMID: 12907567. doi:10.1378/chest.124.2.735
- Miyazawa T, Miyazu Y, Iwamoto Y, et al. Stenting at the flow-limiting segment in tracheobronchial stenosis due to lung cancer. *Am J Respir Crit Care Med*. 2004;169(10):1096–1102. PMID: 15132959. doi:10.1164/rccm.200312-1784OC
- Tang M, Huang LL, Du QQ, et al. Ginsenoside 3β-O-Glc-DM (C3DM) enhances the antitumor activity of Taxol on Lewis lung cancer by targeting the interleukin-6/Jak2/STAT3 and interleukin-6/AKT signaling pathways. *World J Tradit Chin Med*. 2020;6:432–440. doi:10.4103/wjtc.wjtc_51_20
- Handa H, Miyazawa T, Murgu SD, et al. Novel multimodality imaging and physiologic assessments clarify choke-point physiology and airway wall structure in expiratory central airway collapse. *Respir Care*. 2012;57(4):634–641. PMID: 22005343. doi:10.4187/respcare.01363
- Miller RD, Hyatt RE. Obstructing lesions of the larynx and trachea: clinical and physiologic characteristics. *Mayo Clin Proc*. 1969;44(3):145–161. PMID: 5776050.
- Wang JJ. *Respiratory Mechanics*. Beijing: Science Press; 1988:4.35–37.
- Dawson SV, Elliott EA. Wave-speed limitation on expiratory flow—a unifying concept. *J Appl Physiol Respir Environ Exerc Physiol*. 1977;43(3):498–515. PMID: 914721. doi:10.1152/jappl.1977.43.3.498
- Huang GF, Li JH, Huang JJ. Application of the wave-speed theory to analysis of mechanical mechanism for configuration of F-V curve in normal humans. *J West China Univ Med Sci*. 1995;26(3):304.

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