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Assessment of central airway obstruction using impulse oscillometry before and after interventional bronchoscopy

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Abstract

Background: Spirometry is used to physiologically assess patients with central airway obstruction (CAO) before and after interventional bronchoscopic procedures but is not always feasible in these patients, does not localize the anatomic site of obstruction and may not correlate with patients' functional impairment. Impulse oscillometry (IOS) may overcome these limitations. We aimed to assess the correlation of IOS measurements with symptoms and type of airway narrowing before and after interventional bronchoscopy. A secondary objective was to determine whether IOS parameters could discriminate between fixed and dynamic CAO.

Methods: Twenty consecutive patients with CAO underwent spirometry, IOS, computed tomography (CT), MMRC Dyspnea Scale assessment and bronchoscopy before and after interventional bronchoscopy. The collapsibility index (CI) was calculated using morphometric bronchoscopic images on inspiration and expiration during quite breathing to distinguish fixed from variable CAO. The CI in variable CAO was defined as greater than 50% of the luminal area, whereas the CI in fixed CAO was defined as less than 50% of the luminal area. The degree of obstruction was analyzed by CT measurements.

Results: After interventional bronchoscopy, all IOS measurements significantly improved, especially resistance (R5), which decreased from 0.67±0.29 kPa/(l/s) to 0.38±0.17 kPa/(l/s) ($p<0.001$), and reactance

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(X20), which increased from -0.09±0.11 to 0.03±0.08 ($p<0.001$). R5, R5-R20 and X5 changes but not spirometry measurements correlated with changes in MMRC Dyspnea Scale. The type of obstruction correlated with the MMRC Dyspnea Scale and showed distinct IOS measurements.

Conclusions: IOS measurements correlate with improvement in symptoms post intervention. IOS might be useful to discriminating variable from fixed stenosis.

Key words: impulse oscillometry, respiratory resistance, respiratory reactance, morphometric bronchoscopy, central airway obstruction, airway stents

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Introduction

The traditional assessment of central airway obstruction (CAO) involves spirometry, bronchoscopy, and computed tomography (CT).[1-5] From physiologic standpoint, results from published studies show that pulmonary function tests are useful in the diagnosis of CAO and that flow-volume curves can detect and distinguish variable and fixed CAO.[6,7] In addition to diagnosis, however, the localization of flow limiting segments (aka choke points) is relevant for treatment decisions in all cases of CAO (fixed or dynamic). In a previous study, we identified flow limiting segments in the central airways using a combination of flow volume curves, bronchoscopy, endobronchial ultrasonography (EBUS) and CT.[5] More recently, we described how novel multimodality imaging studies and physiologic studies can be used to assess airway wall structure, identify changes in flow-limiting segments before and after treatment, and provide further insights into the pathogenesis of expiratory central airway collapse.[6] Spirometry, however, is not always feasible in patients with CAO due to a variety of patient-related factors, which do not allow or interfere with an optimal forced expiratory maneuver. These include but are not limited to severe dyspnea, cough, fatigue, language barrier, cooperation or cognitive impairment. Furthermore, in patients with CAO, flow volume curves become characteristic when severe obstruction occurs[8] and spirometry values may not

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correlate with the degree of airway narrowing.[9, 10] Even when diagnostic for CAO, spirometry is not able to anatomically localize the site of obstruction, relevant for treatment decisions.[5]

Impulse oscillometry (IOS) is a type of forced oscillation technique that enables pulmonary function tests to be performed during quiet breathing [11, 12] IOS is also effort independent during which brief random pressure pulses of 5 to 35 Hz generated by a small loudspeaker mounted in series with a pneumotachygraph are applied during tidal breathing. Pressure-flow oscillations are superimposed on the subject's tidal breaths, and real-time recordings are used to provide an estimate of total respiratory system impedance, including measurements of resistance (R) and reactance (X) at different frequencies that might differentiate between central and peripheral components of airway obstruction.[12] The 5 Hz signal has slower cycle time and a larger wavelength so it reaches the periphery of the lung providing information about the entire respiratory tract. The 20 Hz signal, on the other hand, has faster cycle time and a shorter wavelength. This signal provides information about the proximal, larger airways. Therefore, an increased R at a low oscillation frequency (5Hz) reflects an increase in total respiratory resistance suggestive of airway obstruction such as that found in patients with COPD, while an increase at a higher frequency (20 Hz) reflects more specifically increased central airway resistance such as that found in patients with CAO due to a variety of causes[13]. This technique was introduced in 1956 to measure respiratory resistance (Rrs)

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and respiratory reactance (Xrs) in humans[14] and has been employed to assess peripheral airway obstructions in patients with chronic obstructive pulmonary disease (COPD) and asthma in children and adults. In case reports and small case series, this technique was proved to be feasible for detecting CAO.[15-18]

In this study, we aimed to assess the correlation of IOS measurements with symptoms and type of airway narrowing before and after interventional bronchoscopy. A secondary objective was to determine whether IOS parameters could discriminate between fixed and dynamic CAO.

Patients and Methods

Study design

This is an analysis of prospectively collected data between April 2008 and December 2010. All patients were consented and enrolled in the study and underwent IOS, spirometry, the dyspnea index, and chest CT before and after the intervention. Twenty consecutive patients with CAO confirmed by bronchoscopy and chest CT were recruited at St Marianna University in Kawasaki, Japan. The site of maximal obstruction in the 20 patients was identified in the trachea and at the level of main carina. All patients underwent IOS, spirometry, MMRC Dyspnea Scale assessment and CT before and after bronchoscopic intervention aimed at restoring airway patency. Twenty-five patients with CAO were

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excluded from our analysis; in 12 patients IOS could not be performed because of the presence of indwelling tracheotomy tubes (n=11) or endotracheal tube (n=1); the other 13 patients didn't have IOS measurements both before and after intervention. These 13 patients with missing IOS measurements could not perform IOS or any pulmonary function testing because of critical airway obstruction requiring emergent intervention. No patients were excluded because of language barrier or cognitive impairment. The ethics committee of St. Marianna University School of Medicine approved this study and all participating subjects gave informed consent.

Methods

This study was registered with the Medical Information Network (UMIN ID000005322). Spirometry and flow-volume curve were performed according to the protocols of the European Respiratory Society (ERS).[19] Forced vital capacity (FVC), forced expiratory volume in one second (FEV1), peak expiratory flow (PEF), forced expiratory flow at 50% (FEF50%) and forced expiratory flow at 25% (FEF25%) were measured using a FUDAC-77 device (Fukuda Electronics, Tokyo, Japan). IOS was performed using Masterscreen IOS (CareFusion, Hochberg, Germany) according to ERS protocols.[19] IOS was carried out before spirometry because forced expiration can affect resistance (Rrs) and reactance (Xrs). Subjects were seated upright with their hands cradling their cheeks during quiet breathing for at

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least five breaths. Pressure pulses, including frequency components from 5 to 35 Hz, were generated by a small loudspeaker and were applied at the subject's mouth. We evaluated the following IOS parameters: R5 (respiratory resistance at 5 Hz), R20 (respiratory resistance at 20 Hz), R5-R20 (difference of R5 and R20), X5 (reactance at 5 Hz), X20 (reactance at 20 Hz) and Fres (resonant frequency).

All patients underwent computed tomography (CT) scanning with a 64-detector CT scanner (Aquilion-64; Toshiba Medical, Tokyo, Japan). CT was performed during a breath hold at deep inspiration for all patients in the supine position. The cross-sectional area (CSA) at the narrowest segment was measures using the Ziostation pulmonary workstation (Ziosoft, Tokyo, Japan) before and after interventional bronchoscopy.[20]

The degree of dyspnea was measured with the use of the modified Medical Research Council (MMRC) Dyspnea Scale. The scores range from 0 to 4, with a score of 0 indicating shortness of breath with strenuous exercise and a score of 4 indicating that the patient is breathless when dressing [21].

All patients were intubated with a rigid bronchoscope (EFER, La Ciotat, France) under general anesthesia. Rigid and flexible bronchoscopy (BF-1T260, BF-P260 and BF-XP260; Olympus Tokyo, Japan) were performed on all patients to assess the narrowest airway segment during spontaneous breathing. Variable and fixed CAO were classified using morphometric bronchoscopy at the narrowest

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segment.[22] The luminal area at the narrowest segment was calculated after the bronchoscopic procedure using the image analysis software (Image J), and the collapsibility index (CI) was defined as the difference in the airway lumen size between inspiration and expiration. CI in variable CAO was defined as greater than a 50% difference in the airway lumen size between inspiration and expiration, and the CI in fixed CAO was defined as less than a 50% difference in the airway lumen size between inspiration and expiration.[22]

Statistical analysis

All analyses were performed using SAS software (release 8.2; SAS Institute, Cary, NC). Results are presented as means ± SD. The difference between variable and fixed CAO was analyzed using Mann-Whitney U test. Pulmonary function measurements and CSA at the narrowest segment were analyzed using a non-parametric Wilcoxon signed rank test before and after interventional bronchoscopy. Significance was established at a $p<0.05$ (two-tailed). Correlation between pulmonary function measurement changes and MMRC (Modified Medical Research Council) Dyspnea Scale were evaluated using Spearman correlation test.

Results

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Patients

Twenty patients (16 male and 4 female) with a mean age of 59.1±14.3 years, a mean body weight of 52.3±13.4 kg and a mean height of 161.9±7.7 cm were enrolled. Three patients with benign variable CAO had tracheomalacia due to relapsing polychondritis and post-tuberculosis stricture. Seven patients had variable CAO and malignant disease with extrinsic compression resulting from primary tumor and associated enlarged lymph nodes. Ten patients with fixed CAO had malignant disease (four lung cancers, four esophageal cancers, one tracheal cancer and one adenoid cystic carcinoma). Eighteen patients required stent insertion. For the two patients without stent placement, 1 required balloon dilation and the other required argon plasma coagulation.

Symptoms and pulmonary function before and after interventional bronchoscopy

After the therapeutic bronchoscopy, MMRC Dyspnea Scale decreased from 3.0±0.6 to 1.5±0.5 (p<0.001), and the airway lumen CSA at the narrowest segment using CT significantly increased from 52.3±31.8 m^2 to 101.1±31.3 m^2 (p<0.001) (Table 1). Pulmonary function measurements also significantly improved, especially PEF, which increased from 2.09±0.93 l/s to 4.48±2.05 l/s (p<0.001), R5, which decreased from 0.67±0.29 kPa/(l/s) (p<0.001), and X20, which increased from -0.09±0.11 to 0.03±0.08 (p<0.001). Correlations between pre MMRC Dyspnea Scale and baseline pulmonary function

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measurements are shown in Table 2. There were correlations between pre MMRC Dyspnea Scale before treatment and spirometry values except for FVC, however there were no correlations between ΔMMRC Dyspnea Scale and spirometry values (table 3). The reason for this is that the MMRC Dyspnea Scale had a smaller change because of the 5 points scale and baseline spirometry was different for each CAO patient. As a result, change in spirometry showed variations after treatment.

On the other hand, R5, R5-R20 and X5 were significantly correlated with improved MMRC Dyspnea Scale (Table 3). The reason for this is that baseline IOS was slightly different for CAO patients and the correlation between IOS parameters and MMRC Dyspnea Scale before treatment was similar to the correlation between the change in IOS parameters and ΔMMRC Dyspnea Scale. The type of obstruction correlated with the MMRC Dyspnea Scale (P=0.067) (Table 4).

IOS analysis for fixed and variable obstruction

Diagnosis of CAO was made by a combination of chest CT and bronchoscopy. From the 20 patients enrolled in this study, all 20 patients had abnormal flow volume curves. Fifteen and 5 had flow volume curves suggesting fixed and variable obstruction, respectively. We confirmed fixed CAO (n=10) and variable CAO (n=10) by bronchoscopy. The flow volume curve findings, however, showed fixed airway

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obstruction pattern in 15 patients and variable pattern in 5 patients. Namely, of the 10 variable CAO cases confirmed by bronchoscopy, 8 showed fixed obstruction pattern on flow volume curve; of the 10 fixed obstruction cases by bronchoscopy, 3 showed variable obstruction pattern on the flow volume curve. All CAO was intrathoracic and the variable collapse was expiratory in nature.

In one patient with fixed CAO due to invasive tracheal stenosis from lung cancer, the flow-volume curve showed marked reduction of inspiratory and expiratory flow with a plateau (Figure 1A, 1B). IOS findings showed that R20 and R5 had similar increases and that Xrs was within normal range (Figure 1C). After placement of an expanding metal stent, spirometry and IOS findings improved (Figure 1D-F).

In one patient with variable tracheal obstruction due to tracheomalacia with relapsing polychondritis, bronchoscopic findings showed expiratory central airway collapse (Figure 2A), and flow-volume curve analysis showed severe reduction of expiratory flow compared to inspiratory flow (Figure 2B). IOS findings showed that the Rrs spectrum became lower at higher frequencies and that Xrs was reduced into abnormal range (Figure 2C). After placement of a self-expanding metal stent (SEMS), airway patency was restored and pulmonary function measurements showed marked improvement (Figure 2D-F).

A comparison between variable and fixed CAO is shown in Table 4. For R5 and R5-R20, a significant difference was seen between variable and fixed CAO (R5; $p=0.009$, R5-R20; $p<0.001$). R20 showed no

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significant difference between variable and fixed CAO (p=0.189). R5-R20 showed a major difference between variable [0.46±0.14 kPa/(l/s)] and fixed CAO [0.08±0.10 kPa/(l/s)], and a value over 0.21 kPa (l/s) was defined as the threshold for variable CAO (Figure 3A). For reactance, a significant difference in X5 and X20 was seen between variable and fixed CAO (X5; $p<0.001$, X20 $p<0.008$). The sensitivity and specificity of both R5-R20 value and X5 value are 100% using ROC curve. Fres showed an insignificant difference between variable and fixed CAO (p=0.081). X5 showed a marked difference between variable [-0.56±0.43 kPa/(l/s)] and fixed CAO [-0.14±0.05 kPa/(l/s)], and a value under -0.19 kPa (l/s) was defined as the threshold for variable CAO (Figure 3B). Inspiratory and expiratory R5 and X5 were greater in patients with variable CAO than in patients with fixed CAO; however, only minimal changes were seen for the remaining IOS measurements between inspiration and expiration for both variable and fixed CAO.

Discussion

The results of this study demonstrate that IOS is a valuable in addition to spirometry for diagnosis and monitoring patients with fixed and variable CAO before and after bronchoscopic interventions. This technique may be particularly useful for those patients with significant pulmonary

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symptoms (severe dyspnea, cough, stridor, and hemoptysis), profound fatigue, language barriers or cognitive impairment who cannot properly undergo forced expiratory maneuvers. IOS is an effort-independent test performed during tidal breathing, does not cause respiratory fatigue and as suggested by this study, may be more sensitive than spirometry for discriminating variable from fixed CAO. R5-R20 and X5 proved to be valuable markers in discriminating between variable and fixed CAO. For variable CAO, Rrs showed marked frequency dependence, whereas it was nearly constant for all frequencies in fixed CAO. The pattern of frequency dependence of resistance in variable CAO is much like that of an upper airway shunt[i25] or as is seen in patients with COPD in which R5 is higher than R20.[23,26-28] In variable CAO, a compliant central airway allows shunting to occur in higher frequency components but there is a difference between inspiratory and expiratory lower frequency components. In contrast, for fixed CAO, the minimal compliance of the central airway is not sufficient to shunt higher frequency components, thereby keeping resistance high with no difference between inspiratory and expiratory frequency components. The decrease in X5 for variable CAO is consistent with the above discussion. In fixed CAO, lung compliance and central airway resistance mainly determine reactance

[i] When forced oscillations are applied to measure the impedance of the respiratory system, part of the airflow generated by the loudspeaker does not enter the lower airways and is lost in motions of the upper airway walls. This process is called an upper airway shunt which causes changes in the estimation of respiratory impedance

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components. However, reactance components in variable CAO are determined by airway compliance instead of lung compliance, resulting in a decrease of X5 and a resulting difference between inspiratory and expiratory X5.

In this study we used morphometric bronchoscopy to assess the type of CAO and CT to determine the degree of airway narrowing. Morphometric bronchoscopy technique to is useful for defining and quantifying fixed and variable CAO[20,29] but image analysis is not performed real-time but post procedure by using image processing software. Real time quantification of the degree of CAO may be achieved in the future by using stereoscopic bronchoscopy. The CI, as defined in this study, has been previously proposed for tracheomalacia and excessive dynamic airway collapse.[22] For the purpose of this study, we used the CI to differentiate variable and fixed CAO. Variable CAO included tracheomalacia and extrinsic compression of the tumor. Generally, tracheomalacia, which is a form of EDAC, is identified as greater than a 50% reduction in the CSA of the airway between inspiration and expiration. This criterion, however, may lead to significant false positive diagnoses if applied during coughing or forced expiration.[30] We therefore applied the CI on images obtained during spontaneous, tidal breathing.

Results of our study showed that ΔR5-R20 was the most sensitivity and specificity in PFTs.. For example, patients with CAO who have profound weakness or dyspnea from their underlying disease may

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be better candidates for IOS than for spirometry testing. The ability to objectively assess dyspnea in these patients is relevant to decision making process regarding treatment strategies (conservative, minimally invasive, open surgery) as well as for proper documentation and meaningful research. In our study, IOS but not spirometry values correlated with MMRC Dyspnea Scale. These findings are in agreement with other studies from ENT literature that showed that MMRC Dyspnea Scale is highly sensitive to the presence of varying degrees of laryngotracheal stenosis and that there was only weak correlation between MMRC Dyspnea Scale and spirometry variables [8]. Similar observations were found in COPD patients in whom there is a strong correlation between the MRC scale and disability, but weaker correlations between MRC scale and FEV1 or PEF. IOS may be therefore preferable for these patients not only because of its improved sensitivity, but also because patients with CAO may have circumstances when forced expiratory maneuvers are not feasible.

We also demonstrated limitations of IOS in the study of patients with CAO. For instance, R5-R20 and X5 measurements for variable CAO were similar to those found in patients with severe COPD with tidal expiratory flow limitation, limiting these parameters application in distinguishing severe COPD from variable CAO. The usefulness of IOS in this study was also assumed to be based on the fact that the resistance obtained at a high frequency preferentially reflects the large central airways and therefore, a

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change in the frequency dependence of resistance can be considered to reflect the change in the large or small airways. However, the airway resistance is distributed heterogeneously across the airways, and this heterogeneity may affect low frequencies more than high frequencies, creating an additional source of frequency dependence that, in principle, is not a reflection of airway size. This is exemplified in this study, which showed that frequency dependence of resistance was actually similar to COPD and in some patients with CAO. Another limitation of IOS, similar to any noninvasive physiologic assessment, is the inability to precisely localize the narrowest airway segment responsible for flow limitation. This is especially relevant for those patients with CAO for which the flow limiting segments are difficult to identify such as those patients with EDAC. For this purpose, the use of intraluminal airway pressure catheter measurements distal and proximal to the narrowed airway during tidal breathing allows immediate intraoperative estimation of the physiologic benefits of a particular bronchoscopic interventional procedure.[21]

We did not measure FIF 50, FEF50/FIF50 or FEV1/PEFR. While usually only diagnostic of central/upper airway obstruction in cases of severe airway narrowing, these measurements could have allowed us to define variable and fixed obstruction based on spirometry data and would have potentially permitted correlations with the IOS variables. While the mean FEV1/FVC ratio of 42 prior to bronchoscopic intervention could have suggested underlying obstructive ventilatory impairment such as asthma or COPD,

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we believe that the significant improvement in FEV1/FVC ratio to 70 after the CAO was palliated suggests that the CAO was the main culprit for the spirometry findings and highlights once more, spirometry's lack specificity for detecting CAO. In addition, in COPD, frequency dependence of respiratory resistance is indicating ventilation disturbance and X5 can detect tidal airflow limitation. Tracheobronchomalacia is a typical example of variable obstruction. It remains unclear whether IOS can distinguish between patients with COPD with and without tracheobronchomalacia.

Our study adds to the body of evidence supporting the use of IOS for physiologic assessment of patients with CAO.[15-18] Although IOS may not be the ultimate test to distinguish between small and large airway processes, or the solution to anatomically localize choke points in patients with CAO, it is however non invasive, effort independent, can potentially be used to differentiate fixed from variable obstruction. In addition, it can be useful for monitoring patients with CAO before and after interventional bronchoscopic procedures. Larger scale studies should clarify whether IOS findings are more sensitive than spirometry for differentiating fixed from variable obstruction and determine whether IOS is more sensitive than spirometry for detecting central airway obstruction.

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Figure legends

Figure 1. Before stenting, bronchoscopic image shows a fixed CAO on expiration (A). Flow-volume curve shows a typical pattern of fixed CAO (B). For IOS, R20 displays a similar increase to R5, and respiratory reactance is within normal range (C). After placement of covered expanding metal stent, bronchoscopic imaging shows restored airway patency (D). Flow-volume curve shows major improvement, whereas a slight improvement is seen for IOS (E, F).

Figure 2. Before stenting, bronchoscopic image shows variable CAO on expiration (A). Flow-volume curve shows a pattern of variable CAO; Flow volume loop suggests a fixed obstruction because of airflow limitation both during inspiration and expiration, but in this case, the stenosis was due to tracheobronchomalacia with airway collapse due to relapsing polychondritis, which is a classic type of dynamic intrathoracic airway obstruction, with worsened flow limitation during expiration (B). For IOS, frequency dependence of resistance and the decrease in respiratory reactance are seen in variable CAO (C). After placement of an expanding metal stent, bronchoscopic imaging shows restored airway patency (D). Both flow-volume curve and IOS show improvements (E, F).

Figure 3. Scatter plot of R5-R20 and X5 compared to the collapsibility index. Open diamonds show patients with variable CAO and closed diamonds show patients with fixed CAO. Variable CAO was

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defined as greater than 50% of the collapsibility index, and fixed CAO was defined as less than 50% of the collapsibility index. Patients with variable CAO showed a marked increase for R5-R20 (p<0.001) compared to fixed CAO with a threshold above 0.21 kPa/(l/s) and X5 showed significant differences between variable and fixed CAO (p<0.001) with a threshold below -0.19 kPa/(/l/s).

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Table 1. Pulmonary function measurements, CT findings for the cross-sectional area and MMRC before and after interventional bronchoscopy

n=20	Before	After	p value
Spirometry			
FVC (l)	2.40±0.79	2.74±0.84	0.350
FEV1 (l)	1.10±0.58	1.93±0.74	0.001
PEF (l/s)	2.09±0.93	4.48±2.05	<0.001
FEF50 (l/s)	0.93±0.68	1.87±0.91	0.001
FEF25 (l/s)	0.53±0.37	0.80±0.54	0.126
IOS			
R5 {kPa/(l/s)}	0.67±0.29	0.38±0.17	<0.001
Inspiration	0.65±0.32	0.36±0.18	<0.001
Expiration	0.68±0.30	0.40±0.17	0.001
R20 {kPa/(l/s)}	0.38±0.09	0.30±0.07	0.035
Inspiration	0.36±0.08	0.27±0.07	0.002
Expiration	0,41±0.10	0.32±0.07	0.001
R5-R20 {kPa/(l/s)}	0.27±0.22	0.08±0.13	0.002
Inspiration	0.29±0.28	0.09±0.14	0.005
Expiration	0.26±0.24	0.08±0.13	0.004
X5 {kPa/(l/s)}	-0.35±0.37	-0.15±0.11	0.003
Inspiration	-0.23±0.32	-0.14±0.10	0.012
Expiration	-0.39±0.43	-0.15±0.11	0.004
X20 {kPa/(l/s)}	-0.09±0.11	0.03±0.08	<0.001
Inspiration	-0.10±0.11	0.03±0.08	<0.001
Expiration	-0.10±0.13	0.02±0.10	<0.001
Fres (1/s)	26.20±9.80	15.89±9.42	0.002
CT measurement			
CSA (m^2)	52.3±31.8	101.1±31.1	<0.001
MMRC	2.95±0.6	1.45±0.5	<0.001

Post intervention, all patients with CAO maintained airway patency, variable obstruction disappeared and thus the results are reported for the entire group; FVC = forced vital capacity; FEV1 = forced expiratory volume at 1 s; PEF = peak expiratory flow; FEF50 = forced expiratory flow after 50%; FEF25 = forced expiratory flow after 25%; R5 = respiratory resistance at 5 Hz; R20 = respiratory resistance at 20 Hz; R5-R20 = difference of R5 and R20; X5 = respiratory reactance at 5 Hz; X20 = respiratory reactance at 20 Hz; Fres = resonant frequency; CSA = cross-sectional area; MMRC = modified medical research council.

Data are shown as mean ± SD. Statistical significance obtained using Wilcoxon signed rank test.

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Table 2. Correlation between pre MMRC Dyspnea scale and Pulmonary function tests

	Pre MMRC Dyspnea Scale (2.95±0.6)	
Spirometry	r value	p value
FVC	-0.307	0.189
FEV1	-0.582	0.007
PEF	-0.687	<0.001
FEF50	-0.583	0.007
FEF25	-0.446	0.049
IOS		
R5	0.742	<0.001
Inspiration	0.701	<0.001
Expiration	0.728	<0.001
R20	0.434	0.056
Inspiration	0.451	0.046
Expiration	0.531	0.016
R5-R20	0.743	<0.001
Inspiration	0.688	<0.001
Expiration	0.693	<0.001
X5	-0.675	0.001
Inspiration	-0.531	0.016
Expiration	-0.728	<0.001
X20	-0.708	<0.001
Inspiration	-0.681	<0.001
Expiration	-0.764	<0.001
Fres	0.639	0.002

Pre intervention MMRC scores were compared with baseline spirometry and IOS values. MMRC = modified medical research council; FVC = forced vital capacity; FEV1 = forced expiratory volume at 1 s; PEF = peak expiratory flow; FEF50 = forced expiratory flow after 50%; FEF25 = forced expiratory flow after 25%; R5 = respiratory resistance at 5 Hz; R20 = respiratory resistance at 20 Hz; R5-R20 = difference of R5 and R20; X5 = respiratory reactance at 5 Hz; X20 = respiratory reactance at 20 Hz; Fres = resonant frequency. Correlation tested by Spearman correlation test. Significance was established at a $p<0.05$ (two-tailed).

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Table 3. Correlation between changes (Δ) in dyspnea score and pulmonary function tests

	ΔMMRC Dyspnea Scale (Mean ± SD -1.5±0.8)		
Spirometry	Mean ± SD	r value	p value
ΔFVC	0.34±0.70	0.337	0.147
ΔFEV1	0.83±0.81	0.073	0.761
ΔPEF	2.39±1.87	0.110	0.646
ΔFEF50	0.95±0.91	0.016	0.948
ΔFEF25	0.28±0.42	-0.224	0.342
IOS			
ΔR5	-0.29±0.22	-0.628	0.003
Inspiration	-0.29±0.22	-0.639	0.002
Expiration	-0.28±0.27	-0.561	0.010
ΔR20	-0.09±0.10	-0.279	0.234
Inspiration	-0.08±0.09	-0.246	0.296
Expiration	-0.10±0.11	-0.214	0.364
ΔR5-R20	-0.19±0.17	-0.625	0.003
Inspiration	-0.20±0.18	-0.649	0.002
Expiration	-0.19±0.21	-0.532	0.016
ΔX5	0.21±0.27	0.641	0.002
Inspiration	0.18±0.24	0.556	0.011
Expiration	0.24±0.34	0.678	0.001
ΔX20	0.12±0.08	0.617	0.004
Inspiration	0.13±0.09	0.400	0.081
Expiration	0.12±0.12	0.609	0.004
ΔFres	-10.61+7.73	-0.314	0.177

The change in MMRC score was compared with changes in spirometry and IOS values. MMRC = modified medical research council; FVC = forced vital capacity; FEV1 = forced expiratory volume at 1 s; PEF = peak expiratory flow; FEF50 = forced expiratory flow after 50%; FEF25 = forced expiratory flow after 25%; R5 = respiratory resistance at 5 Hz; R20 = respiratory resistance at 20 Hz; R5-R20 = difference of R5 and R20; X5 = respiratory reactance at 5 Hz; X20 = respiratory reactance at 20 Hz; Fres = resonant frequency. Correlation tested by Spearman correlation test. Significance was established at a $p<0.05$ (two-tailed).

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Table 4. MMRC, pulmonary function measurements and collapsibility index (CI) for variable and fixed CAO before interventional bronchoscopy

	Variable CAO (n=10)	Fixed CAO (n=10)	*P* value
MMRC	3.3±0.5	2.6±0.52	0.011
FVC (l)	2.09±0.61	2.71±0.86	0.141
FEV1 (l)	0.81±0.39	1.39±0.62	0.026
PEF (l/s)	1.64±0.57	2.54±1.02	0.039
FEF50 (l/s)	0.56±0.40	1.29±0.73	0.014
FEF25 (l/s)	0.39±0.31	0.66±0.39	0.112
R5 {kPa/(l/s)}	0.88±0.23	0.45±0.12	0.001
Inspiration	0.77±0.29	0.43±0.12	<0.001
Expiration	0.89±0.26	0.46±0.13	0.001
R20 {kPa/(l/s)}	0.40±0.09	0.36±0.09	0.384
Inspiration	0.37±0.08	0.34±0.08	0.289
Expiration	0.44±0.10	0.38±0.10	0.173
R5–R20 {kPa/(l/s)}	0.46±0.14	0.08±0.05	<0.001
Inspiration	0.50±0.26	0.09±0.05	<0.001
Expiration	0.45±0.20	0.08±0.05	<0.001
X5 {kPa/(l/s)}	-0.56±0.43	−0.14±0.05	<0.001
Inspiration	-0.51±0.37	-0.14±0.04	<0.001
Expiration	-0.65±0.48	-0.13±0.08	<0.001
X20 {kPa/(l/s)}	-0.17±0.10	−0.01±0.05	0.002
Inspiration	-0.18±0.10	-0.02±0.05	0.001
Expiration	-0.19±0.12	-0.01±0.06	0.003
Fres (1/s)	32.04±8.23	20.29±7.63	0.009
CI (%)	75.8±14.5	12.0±9.3	<0.001

FVC = forced vital capacity; FEV1 = forced expiratory volume at 1 s; PEF = peak expiratory flow; FEF50 = forced expiratory flow after 50%; FEF25 = forced expiratory flow after 25%; R5 = respiratory resistance at 5 Hz; R20 = respiratory resistance at 20 Hz; R5-R20 = difference of R5 and R20; X5 = respiratory reactance at 5 Hz; X20 = respiratory reactance at 20 Hz; Fres = resonant frequency; CI = collapsibility index.

Data are shown as mean ± SD. Group differences were tested with the Mann-Whitney U test.

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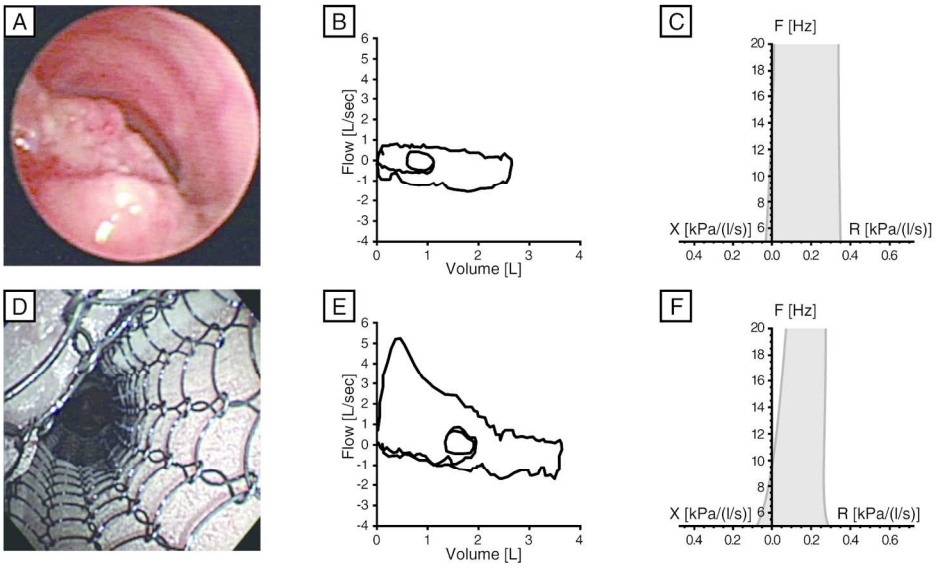

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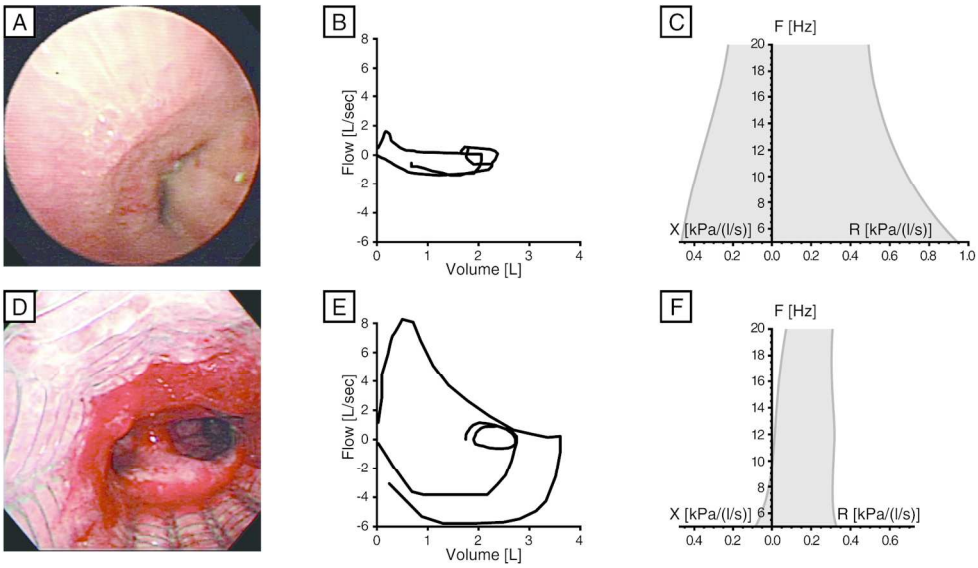

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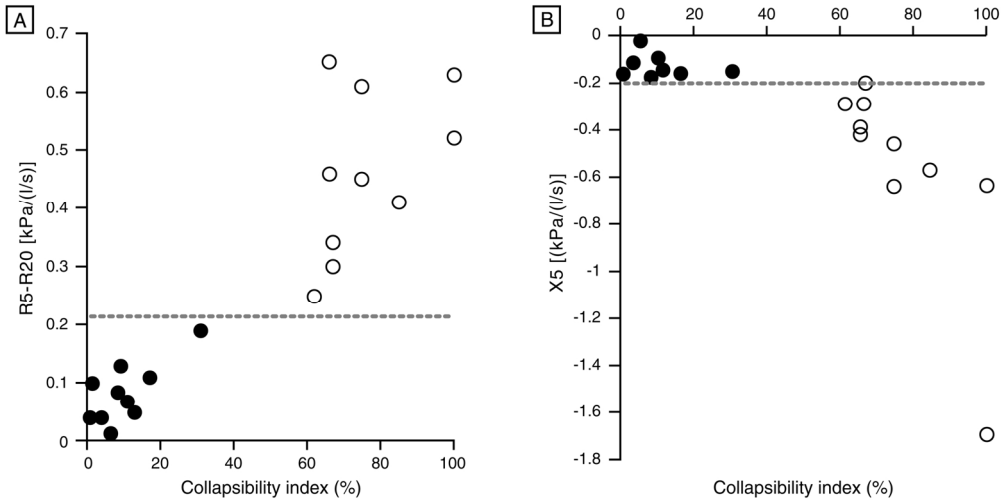

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