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Role of the impulse oscillometry in the evaluation of tracheal stenosis

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Abstract

Introduction and objectives: Tracheal stenosis is a rare and challenging disease. Bronchoscopy is the gold standard for diagnosis and assessment but brings inherent risks. Spirometry is commonly used to access obstructions but is not always feasible due to patient related factors. We therefore considered impulse oscillometry (IOS) as a non-invasive method to quantify airway obstruction and its potential use for diagnosis and follow-up of tracheal stenosis.

Materials and methods: Patients with confirmed tracheal stenosis were recruited between January 1st, 2015 and December 31st, 2016. Before bronchoscopy, all subjects underwent IOS and spirometry; for patients submitted to interventional bronchoscopy the same techniques were also performed after the procedure. We assessed the correlation between IOS measurements and airway narrowing as well as between IOS and spirometry values.

Results: Twenty-one patients were included. Tracheal narrowing was inversely correlated with X5% (r −0.442, p 0.045) and positively correlated with FEV1/PEF (r 0.467, p 0.033). The stenosis length was inversely correlated with PEF and PEF% (r −0.729, $p = 0.001$ and r −0.707, $p = 0.002$, respectively). There was a strong correlation between spirometric and IOS values. We did not find any significant differences between pre- and post-intervention IOS values for patients assessed after interventional bronchoscopy.

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Conclusions: Our study showed a weak correlation between X5% and tracheal narrowing making it unclear whether IOS can be used for physiological assessment of patients with tracheal stenosis. Stenosis length correlated with PEF making it a potential predictor of successful surgical approach. The correlation between IOS and spirometric values makes IOS a potential alternative in patients with suspected tracheal stenosis who are not able to perform spirometry. Larger scale studies should clarify the role of IOS in this pathology.

Introduction

Laryngotracheal stenosis refers to a heterogeneous myriad of rare disorders that cause abnormal narrowing of the central air passageways between the larynx and carina.[1] The problem is rare and challenging and may be congenital or acquired. The majority of cases of acquired laryngotracheal stenosis result from endotracheal intubation; the reported incidence of tracheal stenosis following tracheostomy and laryngotracheal intubation ranges from 0.6% to 21% and 6% to 21%, respectively[2-4] but only 1–2% of these patients are symptomatic or have severe stenosis.[5-7]

Bronchoscopy is considered the gold standard for the diagnosis and assessment of airway abnormalities, including those due to endotracheal intubation.[8] Although it provides direct visualization of the airway, it is an invasive procedure with its inherent risks.

Inspection of the maximal expiratory and inspiratory flow volume loops is currently the simplest and most widely used method to detect the presence of upper airway obstruction (UAO) including tracheal stenosis. Spirometry, however, is not always feasible in patients with UAO, due to patient-related factors that do not allow or interfere with an optimal forced expiratory manoeuvre (e.g. severe dyspnoea, cough, fatigue, language barrier, cooperation and cognitive impairment). Furthermore, significant changes in spirometry appear relatively late in the course of the upper airway narrowing process[9] and spirometry values may not correlate with the degree of airway narrowing.[10,11] These observations indicate the need for a method that can detect UAO and specifically tracheal stenosis in high risk patients.

Impulse oscillometry (IOS) was developed by Michaelson et al.[12] and was based on the physiologic concepts of the forced oscillation technique (FOT) originally described by Dubois et al. in 1956.[13] This non-invasive method requires minimal patient collaboration and provides an estimate of respiratory system impedance and its components (resistance and reactance) at different frequencies. The data can be collected rapidly and the equipment is easy to operate.[14] Compared to forced expiration parameters, IOS could play an important role in cases of tracheal stenosis, even in stable and normally breathing patients, considering the important distortions of the airway, which are deeply affected by forced manoeuvres.

In view of the considerable burden caused to the patient by bronchoscopy and the time needed for the examination, we looked for a non-invasive way of quantifying airway obstruction that could serve as a potential screening and follow-up method. So the aim of the present study was to assess the correlation between IOS measurements and airway narrowing evaluated by bronchoscopy. We also assessed the correlation between IOS and spirometry values and compared those parameters in the patients submitted to interventional bronchoscopy before and after the procedure.

Methods

Subjects

Patients with confirmed tracheal stenosis were consecutively recruited at our Centre between January 1st, 2015 and December 31st, 2016. Before the bronchoscopy, all the subjects underwent IOS and spirometry.

The ethics committee of Centro Hospitalar Vila Nova de Gaia/Espinho approved this study.

Bronchoscopy

All bronchoscopy procedures were performed under sedation managed by an anaesthesiologist, and by an experienced bronchoscopist. In most cases, a flexible bronchoscopy was performed first and if tracheal dilatation was needed the procedure was converted to rigid bronchoscopy and anaesthetic procedures were performed accordingly.

The requirements for patients being submitted to the procedure were in accordance with the standard of care protocol in our institution. Before the procedure, risks and possible complications were explained to each patient and an informed consent was obtained. During bronchoscopy, the pneumologist estimated the percentage of lumen narrowing and the length of the tracheal stenosis through visual inspection; two bronchoscopists jointly performed and confirmed each measurement in all cases. Endoscopic dilatation was performed with insertion of progressively larger rigid bronchoscopes. In some cases diode laser, electro-knife or scalpel were used prior to sequential dilation with rigid bronchoscopes. In some cases in which granulation tissue was persistently observed, topical mitomycin C (1 mg/mL) was applied before finishing the procedure.

Patients presenting chondromalacia, open tracheostomy fistulas and vocal cord paralysis concomitant with the tracheal stenosis and who needed a tracheal prothesis were excluded.

Pulmonary function

Spirometric and impulse oscillation measurements were performed between few hours and one week before bronchoscopy in all patients. In patients who needed interventional bronchoscopy to restore airway patency the same functional measurements were also obtained after the bronchoscopic dilatation of their stenosis, as soon as possible within the first 24 h after procedure.

Pulmonary function tests were conducted using combined spirometry and IOS equipment (Jaeger MS-IOS® Germany). A standardized examination was conducted in all patients according to the protocols of the European Respiratory Society.[15] No premedication prior to the IOS examinations was used.

Nasal clips and manual compression of the cheeks were used to reduce the confounding factors of cheek vibration and escape of air via the nostrils. The tested subject breathed quietly through the mouthpiece with the loudspeaker activated, for 30–45 s without glottis contraction or interposition of the tongue. During that period the loudspeaker emitted about 120–150 pulses that varied between 5 and 35 Hz in frequency and overlap the normal breathing sounds (0.2–2 Hz). We evaluated the following impulse oscillometry parameters: respiratory impedance at 5 Hz (Z5), percentage of predicted impedance at 5 Hz (Z5%), resistance at 5 Hz (R5), percentage of predicted resistance at 5 Hz (R5%), resistance at 20 Hz (R20), percentage of the predicted resistance at 20 Hz (R20%), difference between the resistance at 5 Hz and the resistance at 20 Hz (R 5–20 Hz), reactance at 5 Hz (X5), percentage of predicted reactance at 5 Hz (X5%), and resonance frequency (Rf). Morphology of R or X graphs was also taken in consideration.

Spirometry was conducted immediately after the IOS examination. This technique was carried out before the spirometry because forced expiration could affect resistance and reactance. From the forced expiratory flow-volume curve, we used peak expiratory flow (PEF), forced expiratory flow after expiration of 50% of forced vital capacity (FEF50), forced vital capacity (FVC) and forced expiratory volumes in one second (FEV1); the percentage of predicted PEF (PEF%), FVC (FVC%), FEV1 (FEV1%), midinspiratory forced inspiratory flow (FIF50) and FEV1/PEF and FEF50/FIF50 indices were also obtained.

Statistical analysis

Categorical variables were reported in frequencies (n) and percentages (%). Continuous variables were described as median and range (min–max), as they had no symmetric distribution.

A Mann–Whitney test was used to compare lung function variables between patients presenting chronic obstructive pulmonary disease (COPD) and those who did not.

The correlations between pulmonary function parameters and tracheal narrowing as well as between spirometry and IOS values were evaluated with the Spearman correlation test. A Wilcoxon paired t-test was used to test for significant differences between pre- and postintervention.

The level of significance was set at $p < 0.05$.

Results

Subjects

From a pool of thirty-two patients, we excluded 9 patients who could not perform IOS or any pulmonary function testing because of critical airway obstruction requiring emergency intervention and two patients presenting vocal cord paralysis.

Twenty-one patients were included in the analysis, 11 males (52.4%) and 10 females (47.6%), with a median age of 63 (range, 18–77) and a median body mass index of 25.9 kg/m^2 (range, 21.6–45.8).

The percentage of tracheal $p = 0.057$ lumen narrowing ranged from 10% to 90%. Nine patients (42.9%) presented obstruction of the tracheal lumen >50%. Length of the stenosis varied from 1 to 3 cm.

The majority of the patients (90.5%) presented tracheal stenosis due to prolonged intubation. One patient presented idiopathic tracheal stenosis and another had tracheal stenosis after tracheostomy.

Eleven patients were former smokers and the median pack-years smoked was 20 (range, 2–64); there were no active smokers. Five (23.8%) patients had COPD.

Impulse oscillometry analysis for obstruction

Tracheal stenotic lesions were characterized by a reduction in X5% (r −0.442, p = 0.045). There was no correlation between either Z5, R5, R20, or Rf and the visually estimated percentage of the luminal stricture.

Concerning spirometry, there was a positive low degree correlation between the visually estimated percentage of the luminal stricture and FEV1/PEF (r 0.467, p = 0.033). There was a marginally significant correlation between FEV1 and the visually estimated percentage of the luminal stricture (r −0.422, p = 0.057) (Table 1).

The stenosis length was highly correlated with PEF and PEF% (r −0.729, p = 0.001 and r −0.707, p = 0.002, respectively) but presented no significant relation to any of the IOS values.

Pulmonary function test values did not differ significantly between patients presenting COPD and those who did not.

The direct correlation of spirometric and IOS values showed an inverse moderate to high degree correlation between Z5% and FEV1 (L and %), FVC% and PEF (L/s and %) as well as between R5% and the same parameters. Similarly, MIF50 was strongly correlated with Z5%, R5%, R20 and R20%, X5 and R5-R20 (Table 2).

Pulmonary function before and after interventional bronchoscopy

From the nine patients who could be assessed after interventional bronchoscopy we did not find any significant

Table 1   Correlation between pulmonary function test results and the visually estimated percentage of tracheal stricture.

	R	P
Impedance at 5 Hz, kPa/L/s	0.258	0.259
Impedance at 5 Hz, %	0.035	0.880
Resistance at 5 Hz, kPa/L/s	0.245	0.883
Resistance at 5 Hz, %	0.030	0.883
Resistance at 20 Hz, kPa/L/s	0.282	0.215
Resistance at 20 Hz, %	0.122	0.599
Reactance at 5 Hz, kPa/L/s	−0.030	0.897
Reactance at 5 Hz, %	−0.442	**0.045**
Difference in resistance between 5 Hz and 20 Hz, kPa/L/s	0.090	0.697
Resonance frequency, L/s	0.126	0.587
FEV 1, L	−0.422	**0.057**
FEV 1, %	−0.007	0.974
FVC, L	0.242	0.291
FVC, %	0.123	0.595
PEF, L/s	−0.259	0.258
PEF, %	−0.330	0.330
FEV1/PEF	0.467	**0.033**
FEF50, L/s	0.288	0.205
FIF50, L/s	0.025	0.915
FEF50/FIF50	0.269	0.239

Bold values indicate level of significance $p < 0.05$.
FEV1, forced expiratory volumes in one second; FVC, forced vital capacity; PEF, peak expiratory flow; FEF50, forced expiratory flow after expiration of 50% forced vital capacity; FIF50, midinspiratory forced inspiratory flow.

differences between pre- and post-intervention IOS and spirometric values.

Post-intervention R5 values were lower, although only two patients showed a post-intervention R5 value within normal limits. X5 values increased after intervention (Table 3). There were no relevant changes in the IOS graphs morphology.

Discussion

We have proposed a simple diagnostic tool from IOS, and looked for its validity for tracheal stenosis detection, depending on its severity. So far X5% decreases with increasing tracheal stenosis. We also found that FEV1 (marginal significance) and FEV1/PEF decrease with increasing stenotic area and PEF and PEF% decrease with increasing length of the stenosis.

IOS has been employed to assess peripheral airway obstruction in children and adults with COPD or asthma. There are few studies about its usefulness in detecting UAO.[15–18] In our study X5% was correlated with the tracheal narrowing, decreasing with the increasing stenotic area. Reactance is a reflection of pulmonary elastic capacitance and inertia,[19] and this correlation could be based on the expression of the variable capacitance of the cartilaginous upper airway according to the extension of each lesion. In the study by Handa et al., they assessed the correlations between IOS measurements, symptoms, and type of airway narrowing, before and after interventional bronchoscopy.[16] After interventional bronchoscopy, all IOS measurements significantly improved, especially R5 and X20. Changes in dyspnoea score correlated with R5, R5-20 Hz, and X5.

Our data did not show any significant correlation between resistance and the percentage of tracheal narrowing. Horan et al. evaluated the utility of FOT in patients with central nervous system injuries, for detection and follow-up of post tracheostomy tracheal stenosis.[20] FOT evaluations were compared to tracheal diameter before and after bronchoscopic tracheostenosis dilatation procedures. In this case series the authors found a strong inverse correlation of Rf and Z5 with stenosis diameter and a positive correlation with R5. Although forced oscillation R5 has been reported to increase in patients with UAO,[20] its lack of specificity for UAO detection has also been recognized.[21] In the case of stenosis patients with a smoking history, it is also unclear which part of R is attributable to tracheal obstruction and which part arises from more peripheral obstruction. Handa et al. found that subjects with variable UAO, R5–20 Hz and X5 were similar to those in subjects with severe COPD and tidal expiratory flow limitation[16]; the usefulness of IOS was assumed to be based on the fact that the resistance obtained at a high frequency preferentially reflects the large central airways, and therefore a change in the frequency dependence of resistance can be considered to reflect the change in the large or small airways. Comparing patients with COPD and those without it we did not find significant differences in oscillometry results. In accordance with previous studies,[16,17,20] we observed reductions in resistance and reactance in all patients after each successful dilatation, yet not statistically significant and only in three patients post-intervention R5 values fell within the limits of normal. It is possible that, after an intervention, the combination of residual obstruction and some mucosal swelling due to the procedure itself (e.g., granulation tissue, sputum impaction, development of oedema), may impair a complete resolution

Table 2 Correlations between spirometry and IOS parameters (R; P).

IOS parameters	Spirometry parameters									
	FEV 1	FEV 1%	FVC	FVC%	PEF	PEF%	FEV1/PEF	MEF50	MIF50	MEF50/MIF50
Z5	0.156; 0.498	0.149; 0.518	0.287; 0.207	0.151; 0.512	0.529; **0.014**	0.435; **0.049**	−0.202; 0.380	−0.083; 0.720	−0.392; 0.078	−0.041; 0.987
Z5%	−0.536; **0.012**	−0.709; **<0.001**	−0.346; 0.124	−0.602; **0.004**	−0.643; **0.002**	−0.654; **0.001**	−0.228; 0.320	−0.102; 0.660	−0.789; **<0.001**	0.282; 0.216
R5	0.141; 0.541	0.121; 0.602	0.262; 0.251	0.121; 0.602	0.544; **0.011**	0.441; **0.046**	−0.221; 0.336	−0.074; 0.749	−0.390; 0.081	−0.075; 0.745
R5%	−0.483; **0.027**	−0.661; **0.001**	−0.312; 0.168	−0.577; **0.006**	−0.607; **0.004**	−0.610; **0.003**	−0.207; 0.367	−0.099; 0.669	−0.771; **<0.001**	0.288; 0.205
R20	−0.135; 0.559	−0.019; 0.933	−0.069; 0.766	0.127; 0.585	0.134; 0.562	0.237; 0.301	−0.187; 0.417	−0.101; 0.664	−0.502; **0.021**	−0.039; 0.862
R20%	−0.291; 0.201	−.498; **0.022**	−0.085; 0.714	−0.467; **0.033**	−0.269; 0.238	−0.351; 0.119	−0.166; 0.473	−0.315; 0.165	−0.665; **<0.001**	0.312; 0.169
X5	0.335; 0.137	0.216; 0.438	0.226; 0.325	0.034; 0.882	0.076; 0.743	−0.039; 0.866	0.271; 0.234	0.122; 0.597	0.564; **0.008**	0.094; 0.687
X5%	0.342; 0.129	0.407; 0.067	0.252; 0.232	0.271; 0.235	0.223; 0.331	0.205; 0.373	0.417; 0.60	−0.049; 0.832	−0.006; 0.978	0.029; 0.902
R5−R20	−0.276; 0.225	−0.199; 0.387	−0.222; 0.334	−0.053; 0.821	−0.90; 0.697	0.034; 0.884	−0.223; 0.331	−0.023; 0.920	−0.613; **0.003**	0.149; 0.520
Rf	0.174; 0.450	0.126; 0.588	0.281; 0.218	0.093; 0.688	0.518; **0.016**	0.391; 0.080	−0.176; 0.445	−0.052; 0.823	−0.312; 0.168	0.078; 0.737

Bold values indicate level of significance p < 0.05.
Z5, respiratory impedance at 5 Hz; Z5%, percentage of predicted impedance at 5 Hz; R5, resistance at 5 Hz; R5%, percentage of predicted resistance at 5 Hz; R20, resistance at 20 Hz; R20%, percentage of the predicted resistance at 20 Hz; R5-20%, difference between the resistance at 5 Hz and the resistance at 20 Hz; X5, reactance at 5 Hz; X5%, percentage of predicted reactance at 5 Hz; Rf, resonance frequency; FEV1, forced expiratory volumes in one second; FVC, forced vital capacity; PEF, peak expiratory flow; FEF50, forced expiratory flow after expiration of 50% forced vital capacity; FIF50, midinspiratory forced inspiratory flow.

of resistance to normal values. Despite the limited options to practically and accurately measure the cross-sectional dimensions of subglottic stenosis and quantify the efficacy of treatment, new techniques have emerged. In a recent study the authors performed intraoperative long-range optical coherence tomography (LR-OCT) of the adult airway with objective comparison of pre-intervention and post-intervention luminal patency.[22] OCT is a light-based imaging technique which provides high-resolution, cross-sectional imaging of biological tissue with up to 1–2 mm depth. LR-OCT is a derivative of OCT that is optimized for intraluminal topographical mapping of large, hollow organs such as the airway.[23,24] In the referred study the segmented axial images obtained were coalesced into an array and rendered into 3-D airway models which allowed the surgeon to measure post-dilation changes in the airway and quantify the immediate response to therapy.

Regarding spirometry, we found a positive correlation between FEV1 and FEV1/PEF and the degree of tracheal narrowing. In the studies that additionally to oscillometry also evaluated the correlation of spirometry values with tracheal stenosis size the latter ones did not correlate well.[16,20] Other studies comparing tracheal size, lung function indices and body size in healthy subjects have been published; however, the findings were inconsistent. Some authors found significant correlations between some indices of tracheal size and of lung or body size[25–27]; however the relevant functional indices could differ depending on gender[25] and there were inconsistencies on which lung function index was best correlated with tracheal size.[25,26,28] Other authors found very poor correlations between lung function indices and tracheal size[25,29,30] and they attributed this to the unequal growth pattern of the tracheobronchial tree and the lung parenchyma, which has been coined ''dysanapsis''.[30] The stenosis length was also evaluated and it correlated with PEF and PEF%. Similarly in the study by Jamaati et al., plethysmography variables directly correlated with the intensity and length of stricture.[31] The predicting factors for complications after tracheal resection for benign stenosis were previously evaluated and resections longer than 4 cm were associated with a dramatic rise in the rate of failure.[32,33] Herein, PEF could also be seen as a potential predictor of more challenging surgical approach, predicting lower surgical success rate.

Our results showed a moderate to high correlation between spirometry parameters and IOS parameters mainly impedance and resistance. Similarly, Verbanck et al. found a direct correlation of resistance measurements pre- and postintervention to the corresponding spirometric indices of tracheal stenosis, regardless of respective area lumen size, confirming that spirometry parameters bear a distinct relationship to obstruction in the upper airway.[17] These findings can be of be clinical relevance; for example, patients with tracheal stenosis and profound weakness or dyspnoea may be better candidates for impulse oscillometry than for spirometry, once they cannot perform forced expiratory manoeuvres. Also, IOS may be useful in cases in which spirometry is contraindicated (patients who had recently undergone surgery, who have had recurrent pneumothoraces or who spirometry-related bronchospasm is a concern).

We recognize some limitations in our study. First, the small sample size limits the statistical results. Second, the

Table 3 Features of patients submitted to dilatation and pulmonary function before and after interventional bronchoscopy.

Patient number	Age, years/gender	Before/after dilatation					
		% of tracheal narrowing	R5 (kPa/L/s)	R5 (%)	X5 (kPa/L/s)	X5 (%)	FEV1/PEF (%)
1	76/M	90/40	0.91/0.81	286.70/255.80	−0.78/−0.50	2298.50/1464.80	0.77/0.92
2	69/M	50/20	0.45/0.29	147.10/93.30	−0.14/−0.09	645.40/398.10	0.42/0.28
3	68/F	50/20	0.76/0.62	186.10/152.60	−0.24/−0.21	236.00/210.00	0.84/0.71
4	41/F	30/10	0.56/0.43	154.30/119.50	−0.19/−0.13	520.00/352.70	0.45/0.52
5	77/F	25/10	1.47/1.29	341.60/304.40	−0.45/−0.19	487.00/370.80	0.42/0.73
6	21/M	50/30	0.52/0.41	203.50/158.60	−0.08/−0.07	258.80/230.00	0.60/0.59
7	59/F	70/45	0.78/0.56	199.00/142.00	−0.18/−0.17	226.00/214.00	0.78/0.81
8	63/F	50/40	1.28/0.76	227.8/190	−0.18/−0.23	351.3/254	0.38/0.38
9	67/F	25/10	1.06/0.75	262/186	−0.28/−0.25	289/258	0.27/0.22

Z5, respiratory impedance at 5 Hz; Z5%, percentage of predicted impedance at 5 Hz; R5, resistance at 5 Hz; R5%, percentage of predicted resistance at 5 Hz; R20, resistance at 20 Hz; R20%, percentage of the predicted resistance at 20 Hz; R5-20 Hz, difference between the resistance at 5 Hz and the resistance at 20 Hz; X5, reactance at 5 Hz; X5%, percentage of predicted reactance at 5 Hz; Rf, resonance frequency; FEV1, forced expiratory volumes in one second; FVC, forced vital capacity; PEF, peak expiratory flow; FEF50, forced expiratory flow after expiration of 50% forced vital capacity; FIF50, midinspiratory forced inspiratory flow.

percentage of tracheal narrowing was visually estimated. However, our study design tried to overcome this limitation by having two different bronchoscopists confirming each measurement in all cases and agreeing with it. Lastly, dyspnoea scores were not applied to our population. Assessing dyspnoea in this type of patients can be important as it could be related to the severity of stricture as well as in treatment decision-making.[16]

Conclusion

It remains unclear whether IOS can be used for physiological assessment of patients with tracheal stenosis. Our study showed a weak correlation between X5%, FEV1 and FEV1/PEF and tracheal narrowing. However, stenosis length correlated with PEF making it a potential predictor of more complicated stenosis. Also, the strong correlation between IOS and spirometric values makes IOS a potential alternative in patients with suspected tracheal stenosis who are not able to perform spirometry. Taking into consideration the invasive nature of bronchoscopy, other evaluation method of tracheal stenosis is necessary. Larger scale studies on this subject would be of major importance to further clarify the role of IOS in this pathology.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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