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Oscillometric assessment of airway obstruction in a mechanical model of vocal cord dysfunction

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Abstract

Vocal cord dysfunction (VCD) is characterized by inappropriate adduction of the vocal cords, particularly during inspiration, resulting in obstruction and airflow limitation. Direct visualization of the vocal cords with laryngoscopy is the 'gold standard' for diagnosing VCD. However, it is an invasive technique that may induce airway irritation. The aim of this study was to determine whether the forced oscillation technique (FOT) is useful to estimate the degree of closure of a non-linear orifice under conditions mimicking those found in VCD. The FOT (5 Hz, ± 1 cm H_2O) was applied to an airway model simultaneously with constant levels of flow in the normal breathing range (0–0.8 l/s). Pressure–flow ($P_0 - V'_0$) curves, quasi-static resistance (R_{eff}) and oscillatory resistance (R_{FOT}) were measured in orifices with different areas (0.15–1.12 cm^2) and shapes and in an orifice with variable area. Their pressure-flow relationship followed a quadratic model. Changes in R_{FOT} normalized by flow ($\Delta R_{FOT}/V'_0$) were related to changes in the area of the vocal cord model ($1/A^2_{VC2} - 1/A^2_{VC1}$) from maximum aperture (A_{VC1}) to different degrees of closure (A_{VC2}): $\Delta R_{FOT}/V'_0 = 1.93(1/A^2_{VC2} - 1/A^2_{VC1}) + 2.08$ cm H_2O s^2/l^2; $r^2 = 0.99$. We conclude that FOT could be a useful tool for non-invasively assessing glottic closure in VCD diagnosis, obviating the need for other invasive techniques.

Keywords: Forced oscillation; Respiratory resistance; Airway modelling; Non-invasive monitoring

1. Introduction

Vocal cord dysfunction (VCD) is characterized by airway obstruction and flow limitation during breathing owing to paradoxical adduction of the vocal cords. Diagnosis of VCD is difficult since its clinical symptoms including dyspnoea, shortness of breath and wheezing are common to those typically found in asthma (Christopher et al., 1983). This situation may cause VCD to be mistaken for asthma with the result that many VCD patients are treated unsuccessfully (Newman et al., 1995). Diagnosis of VCD requires assessment of glottic closure during the breathing cycle, e.g. by visualization of the vocal cords with laryngoscopy (Christopher et al., 1983). However, this is an invasive technique that may contribute to upper airways irritation. An alternative procedure for assessing glottic closure could be to estimate upper airway obstruction from the measurement of lung resistance by means of a catheter placed at the oesophagus (Baydur et al., 1982; Condos et al., 1994). Nevertheless, this procedure is not applied in practice since it is invasive and could also induce vocal cord irritation in VCD patients. Therefore, a method for non-invasively assessing glottic closure along the breathing cycle in VCD could be particularly useful for clinical diagnosis.

Airway obstruction can be non-invasively assessed by using the forced oscillation technique (FOT) (Navajas and Farré, 1999). The FOT is based on superimposing a high-frequency (>2 Hz) and low-amplitude (~ 1 cm H_2O) pressure oscillation onto the normal breathing. This is achieved with the patient breathing through a mouthpiece connected to a loudspeaker (Farré et al., 1997). Total respiratory resistance is computed from the oscillatory components of pressure and flow measured at the entrance of the respiratory system. Changes in

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respiratory resistance measured during the breathing cycle can be related to different degrees of upper airway closure since small changes in lung resistance are negligible. Given that FOT allows a continuous and non-invasive monitoring of airways obstruction (Navajas et al., 1998), it could be a useful tool for assessing paradoxical adduction of vocal cords during the breathing cycle.

The VCD is characterized by a reduction in airway calibre at the glottis which can be interpreted as an orifice with a changing opening. This type of airflow obstruction is characterized, in static conditions, by a non-linear pressure–flow relationship. However, at present it is not clear whether oscillatory resistance measured by FOT, i.e. under dynamic conditions, is a suitable estimation of the degree of closure in non-linear resistors. Therefore, we used a mechanical model of the airways to determine whether oscillatory resistance measured by FOT is potentially useful in non-invasively estimating the area reduction in an orifice under conditions mimicking those in VCD.

2. Methods

2.1. Vocal cord dysfunction model

Vocal cords were simulated by an orifice-type resistor based on an almost triangular opening inscribed in a circle with the vertex at the anterior wall (white area in Fig. 1) and inserted in a tube with a 2 cm internal diameter. This geometry, which realistically mimicked the morphology of the vocal cords in the larynx (Brancatisano et al., 1983), was defined by the angle γ and the internal diameter of the tube. Different orifices with areas of 0.15, 0.25, 0.35, 0.50, 0.80 and 1.12 cm^2 ($4^\circ < \gamma < 27^\circ$) were studied. The actual area of each orifice employed was optically determined by a digital camera system (CV-M10BX, JAI, Copenhagen, Denmark). This area range included the usual evolution of vocal cords of a healthy subject during normal breathing (Brancatisano et al., 1983) and the obstructive events found in patients with VCD. To assess the contribution of the orifice shape for a given area, circular orifices with equivalent areas were also used to simulate the vocal cords.

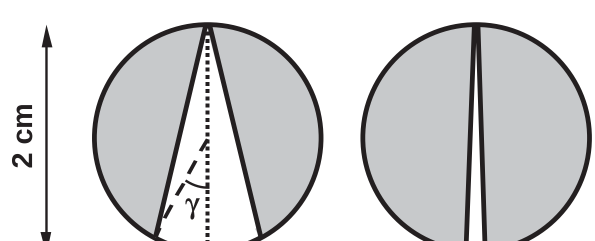

Fig. 1. Orifice resistor mimicking the vocal cords. The area of the orifice (white area) was defined by the angle γ which ranged from 27° during normal spontaneous breathing (A) to 4° during VCD adduction (B).

2.2. Experimental setup

A mechanical model of the respiratory airways was used to reproduce the typical situations found in VCD (Fig. 2). This model consisted of the orifice-type resistor mimicking the vocal cords and a linear mesh-wire resistor (2.53 cm H_2O s/l) accounting for the resistance of the central and peripheral airways. Breathing flow was simulated by a computer-controlled flow generator (PWG; MH Custom Design & Mfg L.C., Midvale, UT, USA) (Fig. 2) based on a servocontrolled pump able to reproduce any constant flow or breathing waveform.

The FOT was applied to the model by an oscillation generator based on a loudspeaker-in-box (JBL-800GTI. 8 in subwoofer, 600W; JBL, Vitoria, Spain). The FOT generator was connected to the airways model to reproduce the measuring conditions in patients: superposition of high-frequency oscillation (FOT) onto a quasi-static breathing flow. Forced oscillation was applied at 5 Hz with a 1 cm H_2O pressure amplitude. Pressure and flow were measured upstream of the orifice with a pressure transducer (MP-45, Validyne, Northridge, CA, USA. The frequency response of the transducers was flat ($\pm 2\%$ in amplitude; $<2^\circ$ in phase lag) over the investigated frequency range (DC-5 Hz)) and a pneumotachograph (Fleisch-II, Metabo, Epalinges, Sweden) connected to a similar pressure transducer. The measured pressure (P) and flow (V') signals were low-pass filtered with an 8-pole Butterworth-type analogue filter (3 dB at 32 Hz). A personal computer with an analogue-to-digital/digital-to-analogue board controlled the generation of the breathing flow and the

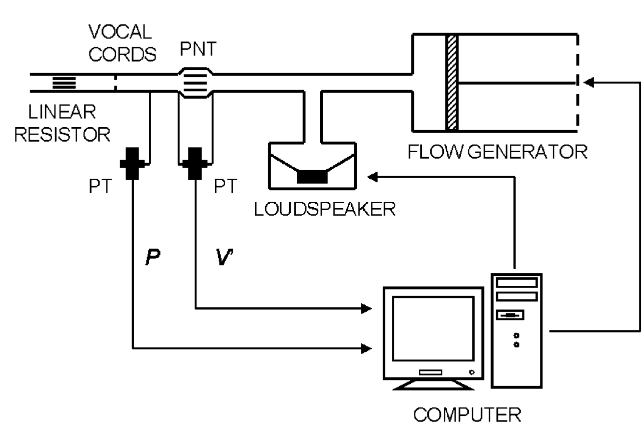

Fig. 2. Experimental setup. FOT was applied to the mechanical model of the respiratory airways superimposed onto different levels of breathing flow. P: pressure; V': flow; PNT: pneumotachograph; PT: pressure transducer.

forced oscillation, and sampled pressure and flow signals at 100 Hz. These signals were recorded for 5 s and digitally low-pass filtered to separate the continuous components (P_0, V'_0) from the 5 Hz oscillatory components (P_{FOT}, V'_{FOT}).

2.3. Measurements

Measurements were performed under two experimental conditions. In the first series of measurements, different levels of constant flow (0–0.8 l/s) reproducing the usual flow values during normal breathing were applied to the airways model to assess the pressure–flow relationship of each orifice. The second series of measurements realistically reproduced the within cycle variations of glottic closure during the obstructive events found in patients with VCD. These variations were simulated by replacing the fixed orifice by a variable orifice based on an iris diaphragm. The moving lever of the diaphragm was attached to the stem of a servocontrolled motor. The diaphragm-motor system was calibrated to determine the relationship between the position of the motor stem and the orifice area. Normal breathing was simulated by a sinusoidal flow waveform with an amplitude of 0.6 l/s and a breathing frequency of 0.2 Hz. Forced oscillations were superimposed onto the breathing pattern. The orifice area varied sinusoidally within a range between 0.09 and 0.47 cm^2, with the same frequency as the breathing flow and with the maximum closure synchronized with mid-inspiration. The area of the orifice was measured simultaneously with the pressure and flow signals by acquiring the position of the motor stem, which was related to the area of the orifice according to the calibration.

2.4. Data analysis

The effective resistance (R_{eff}) of the airways model at constant flow, defined as $R_{eff} = P_0/V'_0$, was computed as the quotient of the continuous components of the measured pressure and flow signals averaged over the 5 s of recorded signals. Oscillatory resistance measured by FOT (R_{FOT}) was computed by fast Fourier transform from the small-amplitude sinusoidal components of pressure (P_{FOT}) and flow (V'_{FOT}) around a given $P_0 - V'_0$ operating point. Accordingly, R_{FOT} corresponded to the first derivative of the pressure/flow relationship with respect to flow ($R_{FOT} = P_{FOT}/V'_{FOT} = \partial P_0/\partial V'_0$).

The pressure–flow ($P_0 - V'_0$) relationship of the vocal cord orifice model was interpreted by means of the non-linear equation $P_0 = k_2 V'_0 2$, where k_2 was a constant accounting for the turbulent flow resistance of the orifice. As described in Doebelin (1975), k_2 was related to the geometry of the orifice by

$$k_2 \propto 1/A_{VC}^2 - 1/A_T^2, \tag{1}$$

where A_{VC} is the area of the vocal cord model (white area in Fig. 1) and A_T is the cross-section area of the tube. The $1/A_{VC}^2$ term may be interpreted as an index accounting for the degree of closure of the vocal cords. Given the contribution of the linear resistance component (k_1) that accounts for the central and peripheral airways resistance, the measured pressure and flow are related by the equation

$$P_0 = k_1 V'_0 + k_2 V'^2_0. \tag{2}$$

Accordingly, effective resistance and oscillatory resistance are

$$R_{eff} = P_0/V'_0 = k_1 + k_2 V'_0, \tag{3}$$

$$R_{FOT} = P_0/V'_0 = k_1 + 2k_2 V'_0. \tag{4}$$

Both resistance indices show a linear dependence on flow, but the slope in the $R_{FOT} - V'_0$ relationship ($2k_2$) is twice the slope in the $R_{eff} - V'_0$ relationship (k_2). According to this non-linear model, the k_1 and k_2 corresponding to each orifice were determined by fitting Eq. (2) to the measured $P_0 - V'_0$ data by least-squares minimization. The measured R_{FOT} values were compared with the ones predicted by model (4) using the values of k_1 and k_2 previously determined for each orifice. Finally, changes in the oscillatory resistance (ΔR_{FOT}) were assessed from the difference between the oscillatory resistance (R_{FOT1}) of the widest orifice of area A_{VC1} (1.12 cm^2) and the oscillatory resistance (R_{FOT2}) of a narrowed orifice of area A_{VC2} ranging from 0.15 to 0.80 cm^2 ($\Delta R_{FOT} = R_{FOT2} - R_{FOT1}$). Combining Eqs. (1) and (4), the changes in R_{FOT} normalized by flow are related to variations in the orifice closure by

$$\Delta R_{FOT}/V'_0 \propto 1/A_{VC2}^2 - 1/A_{VC1}^2, \tag{5}$$

where A_{VC1} is the maximum area of the orifice, i.e. 1.12 cm^2, corresponding to an open glottis and A_{VC2} is the area of the narrowed orifice, i.e. corresponding to the adduction of the vocal cords.

To analyze the data recorded under variable flow conditions, the breathing components of pressure (P_0) and flow (V'_0) were determined by filtering the raw signals with a moving average digital filter (20 points). The oscillatory components of pressure (P_{FOT}) and flow (V'_{FOT}) at 5 Hz were obtained by subtracting V'_0 and P_0 from the raw signals. R_{FOT} was computed by Fourier analysis similar to the constant flow measurements but on a point-by-point basis. The resulting R_{FOT} signal was low-pass filtered with a 2-pole Butterworth digital filter (2 Hz, 3 dB) to smooth the output signal. The time course of the actual oscillatory resistance of the variable orifice was determined in two steps. First, the relationship between the position of the motor stem and the k_1 and k_2 parameters characterizing the different orifice apertures in static conditions was fitted by least-squares minimization. Second, actual oscillatory resistance was computed, on a point-by-point basis, from the k_1 and k_2 values determined for each position of the motor and from the instantaneous flow level according to the model by using Eq. (4).

3. Results

The $P_0 - V_0'$ relationship at constant flow for all the investigated orifices followed a parabolic relationship (Fig. 3A). The $P_0 - V_0'$ relationship of the circular orifice was close to the one corresponding to the almost-triangular orifice with the same area. The mean difference in the pressures between the vocal cord model and the circular orifices of equivalent area was 0.13 cm H_2O. The maximum error was 1.4 cm H_2O for the narrowest orifice at high pressures. Accordingly, the k_1 and k_2 parameters obtained when fitting the non-linear model to the $P_0 - V_0'$ relationship of each orifice were similar for both shapes: $k_1 = 2.02$ and 2.05 cm H_2O s/l and $k_2 = 18.7$ and 18.9 cm $H_2O\,s^2/l^2$ for the vocal cord model and the circular orifices of 0.25 cm^2, respectively. Similar results were found when comparing the other orifices with different shapes but same areas. This indicates that orifice area and not shape is the key factor in determining the $P_0 - V_0'$ relationship.

Oscillatory resistance measured by FOT exhibited a linear dependence on flow with twice the slope of the effective resistance (Fig. 3B). On average, for all the orifices investigated the slope of the dependence of R_{FOT} on V_0' was 2.2 ± 0.4 (mean $\pm$ SD) times the slope in the $R_{eff} - V_0'$ relationship, which is in agreement with the theoretical predictions (3), (4). R_{FOT} measured in each orifice agreed with the oscillatory resistance predicted by the non-linear model (4) using the values of k_1 and k_2 derived from the quasi-static measurements (solid line in Fig. 3B). Similar agreement between measured and predicted R_{FOT} was found when analyzing the results obtained in the vocal cord models with other areas. As expected, the slope of the $R_{FOT} - V_0'$ plots increased when the orifice area was reduced since airflow non-linearities became more important. The mean difference between measured R_{FOT} and the values predicted by model (4) was 5.2% with a maximum of 14% in the wider orifice at low resistance values. Fig. 3B also shows that R_{FOT} was almost independent of the orifice shape for a given area.

Fig. 4 shows how the changes in the degree of orifice closure can be assessed from non-invasive FOT measurements using Eq. (5). This figure, which pools the measured data from all the vocal cord models, shows the relationship between the changes in the oscillatory resistance normalized by flow ($\Delta R_{FOT}/V_0'$) and the

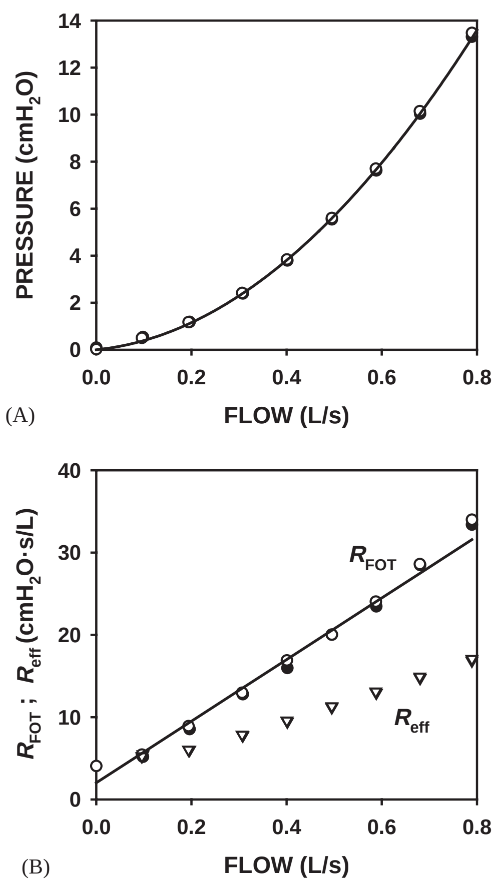

Fig. 3. (A) Quasi-static pressure (P_0)–flow (V_0') relationship in the vocal cord model (closed symbols) and in a circular orifice (open symbols) of same area (0.25 cm^2). Solid line is the non-linear fit (Eq. (2)) of closed symbols. (B) Oscillatory resistance (R_{FOT}; circles) measured by FOT and effective resistance (R_{eff}; triangles) derived from the quasi-static $P_0 - V_0'$ relationship in the same orifice. Solid line is the R_{FOT} predicted using k_1 and k_2 derived from the non-linear $P_0 - V_0'$ relationship of this orifice (A). Closed symbols: vocal cord model; open symbols: circular orifice.

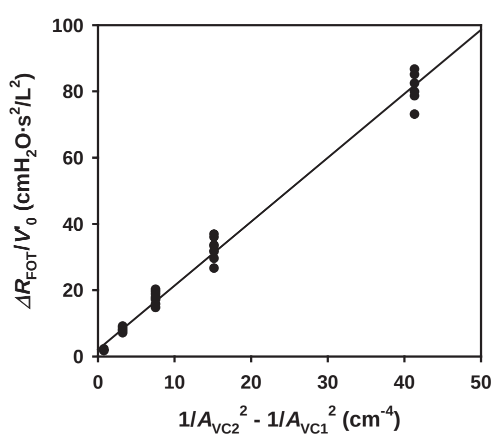

Fig. 4. Changes in oscillatory resistance measured by FOT ($\Delta R_{FOT} = R_{FOT2} - R_{FOT1}$) and normalized by flow ($\Delta R_{FOT}/V_0'$) as a function of changes in orifice closure ($1/A^2_{VC2} - 1/A^2_{VC1}$) for all vocal cord model orifices. A_{VC1}: area of the widest orifice (1.12 cm^2); A_{VC2}: area of the narrowed orifice (from 0.15 to 0.80 cm^2). The solid line is the linear regression fit.

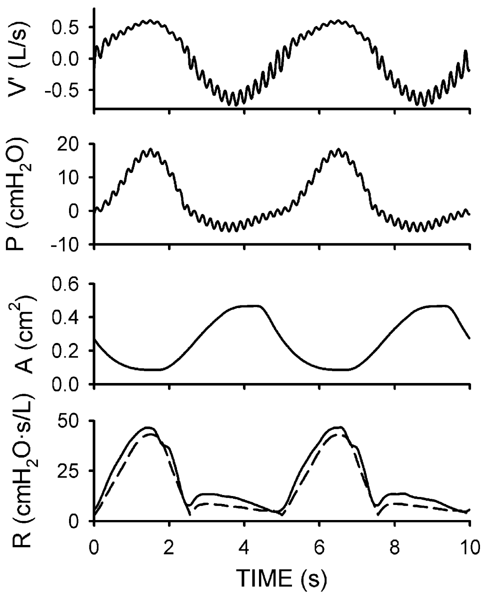

Fig. 5. Example of a measurement of airway obstruction by FOT in a mechanical model of the vocal cords based on a variable orifice. V': flow (positive values correspond to inspiration); P: pressure; A: orifice area; R: airway resistance (solid line: measured by FOT, dashed line: predicted from the model).

changes in the orifice closure ($1/A^2_{VC2}-1/A^2_{VC1}$), where $A_{VC1} = 1.12\,cm^2$. This relationship ($\Delta R_{FOT}/V'_0 = 1.93(1/A^2_{VC2}-1/A^2_{VC1}) + 2.08\,cm\ \ H_2O\,s^2/l^2$; $r^2 = 0.99$) could be used to estimate the degree of closure of the glottis in VCD patients in a non-invasive way.

Fig. 5 shows an example of a FOT measurement under realistic conditions where the area of the glottis varied throughout the breathing cycle. The two top panels show the recorded flow and pressure signals. The figure illustrates how the 5 Hz forced oscillation generated by the loudspeaker was superimposed onto the simulated low-frequency high-amplitude breathing pattern. The third panel in Fig. 5 shows the actual variation of orifice area during the breathing cycle. This situation simulates a severe event with an almost complete closure of the vocal cords during inspiration and an incomplete opening of the vocal cords during expiration. The bottom panel in Fig. 5 shows that the oscillatory resistance measured by FOT reproduced the actual oscillatory resistance predicted by the model from the orifice area and the flow level. Both resistance signals showed transient increases during inspiration (reduced orifice area) and lower values during expiration (Increased orifice area).

4. Discussion

Measurements of oscillatory resistance by the FOT allow the non-invasive estimation of the degree of orifice closure in non-linear conditions similar to those found in VCD. In this study, we employed FOT to measure the oscillatory resistance of an orifice-type resistor mimicking the vocal cords. The static pressure measured in orifices with different areas showed a quadratic dependence on flow that did not depend on the shape of the orifice (Fig. 3A). The oscillatory resistance measured by FOT fulfilled the non-linear theoretical predictions, allowing the non-invasive estimation of the closure of the vocal cord model under dynamic conditions and its effective resistance.

To test the suitability of FOT for non-invasively assessing the degree of closure of the vocal cords, we implemented a mechanical model based on an orifice and a linear resistor accounting for the remaining resistance of the airways. An almost-triangular shape of the orifice (Fig. 1) was selected to realistically simulate the vocal cords geometry. A similar geometry has been used for a numerical simulation of the flow through the human larynx during the breathing cycle (Renotte et al., 2000). To assess the effect of the orifice shape, we also studied circular orifices with an equivalent area. The $P_0 - V'_0$ relationship and R_{FOT} measured in circular orifices showed small differences when compared with the almost triangular model (Fig. 3) with the same area. Thus, when measuring resistance by FOT in VCD patients, it is expected that only the area of the aperture, and not its specific shape, will contribute to the increase in resistance. Since airflow through an orifice-type resistor is essentially turbulent, the pressure drop across the orifice was considered to have a quadratic dependence on flow (Doebelin, 1975). Moreover, it is well known that the resistance of the central and peripheral airways varies during the breathing cycle and it has a non-linear pressure–flow relationship. However, the variation in central and peripheral airways resistance in normal subjects during spontaneous breathing ($\sim 1\,cm\ H_2O\,s/l$) (Peslin et al., 1992; Cauberghs and Van de Woestijne, 1992; Tomalak et al., 1998) is much smaller than the increase in resistance (~ 20–$40\,cm\ H_2O\,s/l$) due to a glottic closure during the symptomatic episodes in patients with VCD. Therefore, the resistance of the central and peripheral airways would make a small contribution to the measured changes in total resistance. Accordingly, for the purpose of this work, central and peripheral airways resistances were considered linear and constant.

Analyzing the results according to (5) (Fig. 4) is particularly useful from the viewpoint of the potential application of FOT in non-invasively diagnosing VCD. This figure, which covers the whole range of values reasonably found in normal breathing and in extremely narrowed vocal cords (resistances of up to 60 cm $H_2O\,s/l$), shows that $\Delta R_{FOT}/V'_0$ was a suitable estimator of the degree of airway closure. When evaluating a patient with VCD by FOT, the changes in respiratory resistance may be measured during the breathing cycle.

During normal breathing, small variations in resistance may be detected due to changes in central and peripheral airways resistance. However, during symptomatic periods of VCD, the high increases in airway resistance could be attributed to an obstruction in the larynx. Even in a patient with both asthma and VCD, the within cycle variations in central and peripheral airway resistance (Officer et al., 1998; Suman et al., 1995) would be smaller than the transient high resistance of the occluded glottis. Therefore, assuming that the within breath changes in central and peripheral airways resistance are minor, any major increase in resistance could be attributed to a reduction in the area of the glottis. Accordingly, the obstructive phenomena found in patients with VCD has been modelled by using an orifice with a variable aperture reproducing the paradoxical adduction of the vocal cords. The oscillatory resistance measured by FOT was able to detect changes in airway obstruction caused by this variable non-linear resistor in agreement with the model prediction (Fig. 5).

In addition to estimating the change in the glottic area, the effective resistance of the glottis during the breathing cycle could be obtained from the oscillatory resistance. In agreement with the theoretical model, when FOT is applied to a linear system (i.e. $k_2 = 0$), R_{FOT} is identical to the R_{eff} measured under quasi-static conditions (3), (4). By contrast, in a non-linear system R_{FOT} differs from R_{eff}, although both resistance indices are related by the simple equation:

$$R_{eff} = R_{FOT}/2 + k_1/2. \quad (6)$$

For the measurements at constant flow, this relationship is illustrated in Fig. 6, which indicates that $R_{FOT}/2$ was a suitable estimator of the effective resistance. Therefore, FOT is a non-invasive method which also allows a simple estimation of the effective resistance in

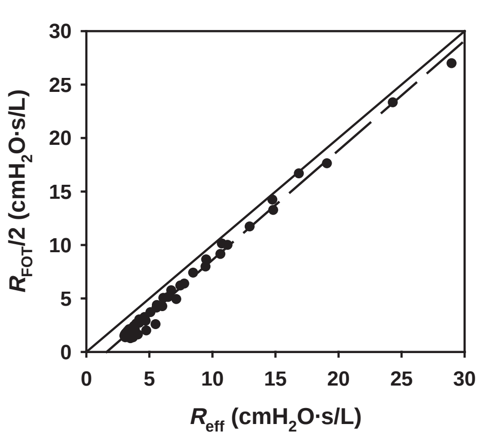

Fig. 6. Non-invasive estimation of effective resistance (R_{eff}) from FOT measurements ($R_{FOT}/2$). Data measured for all vocal cord model orifices and flows are pooled. The solid line is the identity line and the dashed line is the linear regression fit ($R_{FOT}/2 = 1.03R_{eff} - 1.65$ cm H_2O s/l; $r > 0.99$).

non-linear conditions, obviating the need for an invasive oesophageal catheter. Moreover, it is noteworthy that the bias due to the term $k_1/2$ in Eq. (6) is not clinically relevant when assessing high vocal cord adduction. Indeed, this bias is expected to be half the value of the linear component of normal respiratory resistance, i.e. about 1 cm H_2O s/l. This would represent a negligible error in the estimation of abnormally high resistances. Thus, ignoring the $k_1/2$ term during airway resistance measurements in the range 10–30 cm H_2O s/l in VCD patients would induce an error in resistance of only about 3–10%.

The most common FOT applications to assess lung mechanics are based on computing the patient mean oscillatory resistance over a period covering several breathing cycles (typically 16 s) (Navajas and Farré, 1999). With this conventional procedure the statistical robustness of the computed resistance is considerably high since several forced oscillation cycles are included in the computation. Obviously, this statistical stability is obtained at the cost of losing time resolution within the breathing cycle. By contrast, the data analysis employed in this work is focused on the assessment of the changes of patient resistance within the breathing cycle. Accordingly, patient oscillatory resistance is computed on a cycle-by-cycle basis. The cost of such an increase in time resolution is that the resistance values obtained are more affected by measurement noise. However, published results concerning the application of this data analysis on FOT measurements during sleep studies (Farré et al., 1997; Navajas et al., 1998) suggest that this kind of analysis provides reliable resistance values. Given the periodic nature of spontaneous breathing, the reproducibility of the within-cycle resistance values can be improved by averaging the results obtained at specific points of several breathing cycles (e.g. mid-inspiration, mid-expiration) (Farré et al., 1997; Navajas et al., 1998).

Diagnosis of VCD by laryngoscopy may be difficult or impossible during asymptomatic periods. However, some conditions such as emotional stress, exercise (McFadden and Zawadski, 1996) and environmental exposures (Perkner et al., 1998; Shusterman, 1999) have been reported as triggering factors inducing VCD (Christopher et al., 1983). Exercise (McFadden and Zawadski, 1996) and irritant-induced (Perkner et al., 1998) provocation tests could help in the diagnosis of VCD. Nevertheless, application of laryngoscopy for vocal cords visualization during these challenges may be difficult. Since FOT is a non-invasive technique, it could be easily applied in challenge tests to allow the continuous monitoring of the vocal cord obstruction during spontaneous breathing. Therefore, FOT may help to elucidate whether paradoxical adduction of the vocal cords is induced by exercise or irritant agents or by other conditions such as hyperventilation/panic attacks (Shusterman, 2001).

In conclusion, we have demonstrated that the non-linear relationship describing the quasi-static pressure–flow curve in orifices can also be applied to the measuring conditions during FOT application: small-amplitude, high-frequency oscillations superimposed onto high quasi-static flows. Accordingly, this model study suggests that FOT is potentially useful for non-invasively assessing the degree of glottic closure in VCD.

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References

Baydur, A., Behrakis, P.K., Zin, W.A., Jaeger, M., Milic-Emili, J., 1982. A simple method for assessing the validity of the esophageal baloon technique. American Review of Respiratory Disease 126, 788–791.

Brancatisano, T., Collett, P.W., Engel, L.A., 1983. Respiratory movements of the vocal cords. Journal of Applied Physiology: Respiratory Environmental & Exercise Physiology 54, 1269–1276.

Cauberghs, M., Van de Woestijne, K.P., 1992. Changes of respiratory input impedance during breathing in humans. Journal of Applied Physiology 73, 2355–2362.

Christopher, K.L., Wood, R.P., Eckert, R.C., Blager, F.B., Raney, R.A., Souhrada, J.F., 1983. Vocal-cord dysfunction presenting as asthma. New England Journal of Medicine 308, 1566–1570.

Condos, R., Norman, R.G., Krishnasamy, I., Peduzzi, N., Goldring, R.M., Rapoport, D.M., 1994. Flow limitation as a noninvasive assessment of residual upper-airway resistance during continuous positive airway pressure therapy of obstructive sleep apnea. American Journal of Respiratory & Critical Care Medicine 150, 475–480.

Doebelin, E.O., 1975. Measurement Systems: Application and Design. McGraw-Hill, Tokyo, Japan, pp. 465–473.

Farré, R., Peslin, R., Rotger, M., Navajas, D., 1997. Inspiratory dynamic obstruction detected by forced oscillation during CPAP. a model study. American Journal of Respiratory & Critical Care Medicine 155, 952–956.

McFadden, E.R.J., Zawadski, D.K., 1996. Vocal cord dysfunction masquerading as exercise-induced asthma. a physiologic cause for "choking" during athletic activities. American Journal of Respiratory & Critical Care Medicine 153, 942–947.

Navajas, D., Farré, R., 1999. Oscillation mechanics. In: Respiratory mechanics Milic-Emili, J. (Ed.), European Respiratory Monograph. European Respiratory Society Journals Ltd. 4, 112–140.

Navajas, D., Farré, R., Rotger, M., Badia, J.R., Puig-de-Morales, M., Montserrat, J.M., 1998. Assessment of airflow obstruction during CPAP by means of forced oscillation in patients with sleep apnea. American Journal of Respiratory & Critical Care Medicine 157, 1526–1530.

Newman, K.B., Mason, U.G., Schmaling, K.B., 1995. Clinical features of vocal cord dysfunction. American Journal of Respiratory & Critical Care Medicine 152, 1382–1386.

Officer, T.M., Pellegrino, R., Brusasco, V., Rodarte, J.R., 1998. Measurement of pulmonary resistance and dynamic compliance with airway obstruction. Journal of Applied Physiology 85, 1982–1988.

Perkner, J.J., Fennelly, K.P., Balkissoon, R., Bartelson, B.B., Ruttenber, A.J., Wood, R.P., Newman, L.S., 1998. Irritant-associated vocal cord dysfunction. Journal of Occupational & Environmental Medicine 40, 136–143.

Peslin, R., Ying, Y., Gallina, C., Duvivier, C., 1992. Within-breath variations of forced oscillation resistance in healthy subjects. European Respiratory Journal 5, 86–92.

Renotte, C., Bouffioux, V., Wilquem, F., 2000. Numerical 3D analysis of oscillatory flow in the time-varying laryngeal channel. Journal of Biomechanics 33, 1637–1644.

Shusterman, D., 1999. Upper and lower airway sequelae of irritant inhalations. Clinical Pulmonary Medicine 6, 18–31.

Shusterman, D., 2001. Oddor-associated health complaints: competing explanatory models. Chemical Senses 26, 339–343.

Suman, O.E., Babcock, M.A., Pegelow, D.F., Jarjour, N.N., Reddan, W.G., 1995. Airway obstruction during exercise in asthma. American Journal of Respiratory & Critical Care Medicine 152, 24–31.

Tomalak, W., Peslin, R., Duvivier, C., 1998. Variations in airways impedance during respiratory cycle derived from combined measurements of input and transfer impedances. European Respiratory Journal 12, 1436–1441.