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# Tracheal distensibility in cystic fibrosis

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**ABSTRACT: Size and distensibility of large airways have important implications for flow limitation and the efficacy of coughing. From radiological and functional data, some authors have suggested an increased size and distensibility of the trachea in cystic fibrosis (CF).**

**Using computed tomography (CT) we compared size and distensibility of the trachea in 5 cystic fibrosis patients and five age- and height-matched healthy volunteers. Tracheal cross-sectional area was measured 25 mm below the cricoid cartilage. CT recordings were made at functional residual capacity, at 0 and +20 cm$H_2O$ mouth pressure. Inductive plethysmography was used to check that during these manoeuvres lung volume did not change and that the glottis remained open.**

**Tracheal cross-sectional area and derived indices of tracheal distensibility were similar in the two groups.**

**This study does not support the concept of an increased size and distensibility of the trachea in cystic fibrosis.**

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Some years ago, from a radiological study, GRISCOM *et al*. [1], suggested that chronic airways inflammation in cystic fibrosis (CF) may lead to an increased size of the trachea. The authors also suggested that tracheae of CF patients are "abnormally flaccid". This was, however, a retrospective study and controls were from the literature. Large airway size and distensibility may have important implications for flow limitation and ability to cough and clear secretions. Autopsy studies of patients with CF have shown tracheal inflammation [1] and hypertrophy as well as hyperplasia of the mucous glands [1, 2]. Large supramaximal flow transients and decrease of end-expiratory flow rates after bronchodilation were reported in some patients with CF [3–6].

These findings were considered by some authors to reflect "airway instability" and floppy large airways. However, this interpretation of functional data cannot be a substitute for direct measurements of the size and distensibility of large airways. In a recent study, BROOKS [7] used the acoustic reflection technique to measure tracheal size. He concluded that although the tracheal size of patients with CF was not different from that of matched controls at functional residual capacity (FRC), the distensibility of the trachea was increased in the former group. Distensibility of the trachea was, however, assessed indirectly from measurements of airway size at two lung volumes, and no transmural pressure was recorded.

In the present study, we have measured the cross-sectional area (CSA) of the trachea with a computed tomography (CT) scan in patients with CF and healthy subjects. Distensibility of the trachea was derived from measurements of CSA at zero and positive transmural pressures.

## Materials and methods

Five patients (3 females and 2 males) with cystic fibrosis and five age- and height-matched healthy volunteers (3 females and 2 males) were studied. Lung function values, CSA and "distensibility" of the trachea were measured.

Written, informed consent was obtained both from healthy subjects and patients. The experiment was approved by the Ethics Committee of the hospital.

Lung function tests comprised measurements of static and dynamic lung volume, airway resistance ($R_{aw}$) and maximal expiratory flow rates. Subjects were seated in a pressure-corrected whole-body plethysmograph. $R_{aw}$ (measured between 0.5 $L \cdot s^{-1}$ inspiratory and expiratory flows) and thoracic gas volume (TGV) were determined using the method of DUBOIS and co-workers [8, 9]. The sum of the computed TGV and inspiratory capacity yielded the total lung capacity (TLC). To avoid TGV overestimation, panting was performed at less than 1 cycle per second (cps) [10]. During $R_{aw}$ measurements, panting was performed at 2 cps to avoid loop formation. $R_{aw}$ was also expressed as specific airway conductance ($_sG_{aw}$), the reciprocal of $R_{aw}$ divided by TGV. The lung volume used to construct the flow-volume curves was obtained by electronic integration of flow measured at the mouth with a pneumotachograph. Forced expiratory vital capacity (FVC), peak expiratory flow (PEF) and maximal expiratory flow at 25 and 50% of FVC ($V'_{max,25}$ and $V'_{max,50}$, respectively) were measured from photographs of flow-volume curves displayed on a storage oscilloscope.

Signals were also backed-up on tape (TEAC R81 cassette data recorder). Forced expiratory volume in one

second ($FEV_1$) was measured on paper from the lung volume signal recorded *versus* time on a Gould Brush 480 recorder. Four $R_{aw}$ and TLC measurements followed by three reproducible (within 5% of FVC) flow-volume loops were recorded in each subject.

On a separate day, the CSA of the extrathoracic subglottic trachea (at 25 mm below the cricoid cartilage) was measured with a Philips LX CT Scan. Subjects were supine and their head was in neutral position, midway between flexion and extension. Since, in previous training sessions, CF patients could not sustain an even negative pressure, or an even positive pressure larger than +20 $cmH_2O$, measurements of tracheal CSA were restricted to 0 and + 20 $cmH_2O$ mouth pressures. Subjects had been trained to keep the glottis open. Mouth pressure was measured with a Validyne (±140 $cmH_2O$) pressure transducer. To avoid changes in the CSA of the trachea linked to variations in lung volume, all CT images were made at functional residual capacity (FRC). Lung volume was monitored with an inductive plethysmograph (Respitrace), with one band placed around the lower part of the thorax. To verify that the respiratory manoeuvres were performed with an open glottis, the second band of the inductive plethysmograph (a baby size band 2 cm in width) was placed around the upper part of the neck, above the thyroid cartilage. We have previously demonstrated that inductive plethysmography of the neck can record changes in the CSA of the pharyngeal airway when submitted to changes in transmural pressure [11]. With a closed glottis, pressure changes are not transmitted to the pharyngeal airways and no neck CSA changes are recorded. Mouth pressure, and CSA changes of the neck and thorax were simultaneously recorded *versus* time on a Gould ES 1000 electrostatic recorder.

The trachea moves cranially when transmural pressure is positive and caudally when transmural pressure becomes negative. To ensure that tracheal CSA was measured at the same level despite changes in transmural pressure, we performed each measurement at a point relative to the cricoid cartilage. To select the level of section, *i.e.* 25 mm below the cricoid cartilage, a scout lateral radiogram was performed before each CT transversal image. Each image was obtained in 1.9 s. Tracheal images were projected and traced on paper. Measurements of CSA were made with a planimeter after correction for magnification.

Variables were compared with analysis of variance and Newman-Keuls test for multiple comparisons of means.

## Results

Anthropometric and selected pulmonary function data of cystic fibrosis patients and healthy subjects are summarized in table 1. Pulmonary disease of CF patients was moderate to severe, as illustrated by the low $FEV_1$ (41% of predicted value) and Shwachman score (51 out of 100) [12]. All respiratory variables were significantly different between the two groups, except TLC. Table 2 presents, for both groups, tracheal CSA values at 0 and +20 $cmH_2O$ mouth pressure, *i.e.* at zero and +20 $cmH_2O$ transmural pressure since pressure outside the extrathoracic trachea is atmospheric. Two indices of tracheal distensibility were also computed: tracheal "compliance" (changes in CSA divided by changes in transmural pressure); and specific "tracheal compliance" ("tracheal compliance" divided by CSA at zero pressure, which takes into account differences in airway size). All these indices were comparable in the two groups.

Table 1. – Physical and functional data in patients with cystic fibrosis and healthy subjects

| | Cystic fibrosis | Healthy Subjects |
|---|---|---|
| Age yrs | 22±3 | 23±3 |
| Height cm | 163±12 | 167±13 |
| Weight kg | 46±6 | 57±10 |
| $_sG_{aw}$ $cmH_2O^{-1}\cdot s^{-1}$ | 0.09±0.03* | 0.26±0.1 |
| TLC L | 4.53±0.98 | 5.61±1.29 |
| FVC L | 2.38±0.71* | 4.49±1.09 |
| $FEV_1$ L | 1.38±0.63* | 3.57±0.83 |
| $FEV_1$ % pred | 41±15* | 98±4 |
| $V'_{max,50}$ $L\cdot s^{-1}$ | 1.29±0.65* | 4.72±0.16 |

Values are presented as mean±SD. $_sG_{aw}$: specific airway conductance; TLC: total lung capacity; FVC: forced vital capacity; $FEV_1$: forced expiratory volume in one second; $V'_{max,50}$: maximal expiratory flow at 50% of FVC; % pred: percentage of predicted value. *: $p<0.05$, between patients with cystic fibrosis and healthy subjects.

Table 2. – Cross-sectional area (CSA) of the trachea and indices of tracheal distensibility in patients with cystic fibrosis and healthy subjects

| | Cystic fibrosis | Healthy Subjects |
|---|---|---|
| CSA at 0 $cmH_2O$ $cm^2$ | 2.24±0.47 | 2.11±0.46 |
| CSA at +20 $cmH_2O$ $cm^2$ | 2.71±0.74 | 2.52±0.74 |
| "Tracheal compliance" $cm^2\cdot cmH_2O^{-1}$ | 0.023±0.016 | 0.021±0.016 |
| Specific "tracheal compliance" $cmH_2O^{-1}$ | 0.010±0.006 | 0.009±0.006 |

## Discussion

We have measured tracheal CSA in five CF patients and five healthy controls and found it, as well as derived indices of tracheal distensibility, to be comparable in both groups.

Several studies had previously suggested that either the size or the distensibility of the trachea are increased in CF. However, these radiological and functional studies were based on indirect evidence only. Recently, BROOKS [7], using the acoustic reflection technique, had focused on tracheal CSA measurements in CF. He found that near FRC the tracheal size of patients with CF was not different from that of age- and sex-matched control subjects. However, in a subgroup of patients, CSA of the trachea at TLC was significantly larger than that of a control group. The increase in tracheal area per change in lung volume was statistically greater in CF patients. These data were interpreted by the author as evidence of an increased tracheal distensibility in CF.

Because of the discrepancy between our findings and those of BROOKS [7] methodological differences must be considered. CT scan is still regarded as the standard method to measure tracheal area [13]. Although the

acoustic reflection technique has been validated by comparison with the CT scan [13, 14], several potential sources of variability of the acoustic reflection method have been reported [13, 15].

In his study, BROOKS [7] did not record any pressure. As he correctly points out, the lung volume dependence of the tracheal area, which he used to estimate airway distensibility, may at best be considered as an indirect index of airway compliance. Lung disease in the patients studied by BROOKS [7] was less severe than in our patients (mean±SD $FEV_1$ 2.27±0.37 *versus* 1.15±0.38 L, respectively). Since airways instability in CF was mostly described in patients with severe lung disease, this difference cannot explain the different results of the two studies.

Our values of tracheal CSA in controls at FRC under static conditions are in agreement with previous data collected during tidal breathing [13, 15, 16]. Like BROOKS [7], we found no difference between tracheal CSA of CF patients and control subjects at FRC (mean±SD) (BROOKS: 1.99±0.13 *versus* 1.87±0.10 $cm^{2,}$ respectively, present study: 2.24±0.47 *versus* 2.11±0.46 $cm^{2,}$ respectively). In the present study, the mean increase in tracheal CSA from 0 to + 20 $cmH_2O$ mouth pressure was 19% in control subjects and 21% in CF patients. These changes are comparable to those observed in normal subjects by GRISCOM and WHOL [17] and MORENO *et al*. [18], who determined tracheal CSA by CT. Surprisingly, in normal subjects, BROOKS [7] found virtually no difference between tracheal area at FRC (1.90±0.15 $cm^2$) and TLC (1.91±0.13 $cm^2$). An increase in tracheal CSA was found only in patients with CF. This is unexpected and in contrast to previous studies with the acoustic reflection technique [19], CT scan [20], or fibreoptic cinebronchoscopy [21]. Using the CT scan, DOLYNIUK and FAHEY [20] observed on average a 16% increase in extrathoracic (as well as in intrathoracic) tracheal area between FRC and TLC. With the acoustic reflection technique, HOFFSTEIN *et al*. [19] reported an average increase of 25% in extrathoracic tracheal area between residual volume (RV) and TLC.

In conclusion, our results do not support the concept of increased distensibility of the trachea in cystic fibrosis. One can argue that we have studied only a small number of patients with cystic fibrosis. However, taking into account the large interindividual variability of cross-sectional area measurements of the trachea, we have found consistent and strikingly similar results both in cystic fibrosis patients and control subjects.

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