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Lung function, CT-scan and X-ray in upper airway obstruction due to thyroid goitre

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ABSTRACT: The purpose of this study was to assess the clinical reliability and to compare routine lung function tests (maximal flows and resistance) and radiological images (computed tomography (CT)-scan and X-ray) in upper airway obstruction.

We, therefore, performed these examinations prospectively in 28 female patients (aged 68±13 yrs) with a goitre and without pulmonary disorders. Lung function measurements consisted of maximum expiratory and inspiratory flow-volume curves and of airway resistance. CT-scans and X-rays were performed during apnoea at functional residual capacity (FRC).

Peak expiratory flow was 3.6±1.3 $l \cdot s^{-1}$ (*i.e.* 62±21% predicted); airway resistance was 0.38±0.14 kPa (*i.e.* 149±58% pred); and specific conductance was 1.0±0.3 kPa (*i.e.* 70±24% pred). Almost all lung function tests were significantly correlated with each other. On CT-scan the tracheal cross-sectional area at the zone of tracheal narrowing could be evaluated in 26 patients and was 58±17% ($CT_{1/2}$) of the control area 2 cm above the carina (CT_2). On X-ray the sagittal and coronal tracheal diameters at the zone of narrowing could only be measured in 16 subjects and were 60±17% (X-dia$_{1/2}$) of the diameter at the control level. $CT_{1/2}$ and X-dia$_{1/2}$ were significantly correlated to each other. No correlation was found between the lung function tests and the radiological indices except airway resistance and CT_2.

Routine lung function and CT-scan do not provide comparable information on the degree of airway obstruction due to a goitre. Furthermore, X-ray of the trachea seems to be unreliable in visualizing upper airway obstruction.

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Large thyroid goitres generally grow intrathoracically and may cause upper airway obstruction (UAO) [1, 2], or even give rise to acute respiratory failure [2–4]. Routine detection and assessment of UAO is based mainly on radiology (computer tomography (CT)-scan and X-ray) and on lung function tests (spirometry with maximal flow-volume curves and resistance measurements) [5–9].

Comparative studies of tracheal size, lung function indices and body size in healthy subjects have been published; however, the findings were inconsistent [10–19]. Some authors found significant correlations between some indices of tracheal size and of lung or body size [10, 17, 18]; however the relevant functional indices could differ depending on sex [10], and there were, in particular, inconsistencies on which lung function index was best correlated with tracheal size [10, 17–19.] Other authors found very poor correlations between lung function indices and tracheal size [10–12], or between tracheal size and lung or body size [11–16], and they attributed this to the unequal growth pattern of the tracheobronchial tree and the lung parenchyma, which has been coined "dysanapsis" [12].

We are unaware of published data on the relationship between changes in radiological, transverse tracheal dimensions and lung function abnormalities in UAO. It is, therefore, not clear which radiological or lung function measurement is clinically most useful *i.e.* most relevant and reliable in UAO.

The aim of the present study was to evaluate and to compare routinely applicable lung function tests and radiological changes in patients with UAO due to a goitre.

Patients and methods

Patients

Twenty-eight female patients (age 68±13 yrs) with an euthyroid multinodular goitre were evaluated prospectively. The diagnosis had been made by measurement of thyroid stimulating hormone (TSH) and thyroxine (T4) in combination with ultrasonography and/or nuclear imaging of the thyroid.

Patients with a history or clinical evidence of chronic obtructive pulmonary disease (COPD), or asthma or of other pulmonary disorders, including obstructive sleep apnoea syndrome, and smokers were excluded. The selected patients were divided into three subgroups on the basis of the maximal expiratory flow-volume (MEFV) curve and maximal inspiratory flow-volume (MIFV) curve, as described previously [5, 20]: the subgroup with a variable extrathoracic obstruction (n=6) was characterized by an inspiratory plateau on the MIFV curve and a maximal mid-expiratory flow/maximal mid inspiratory flow (MEF_{50}/MIF_{50}) ratio of more than 1.1; in the subgroup with a fixed obstruction (n=11), both inspiratory and expiratory flow plateaus were present with a MEF_{50}/MIF_{50} ratio of 0.9–1.1; the subgroup with a variable intrathoracic obstruction (n=11) presented an expiratory flow plateau with a MEF_{50}/ MIF_{50} ratio of below 0.9.

Methods

The FEV_1, forced expiratory volume in one second (FIV_1) and the MEFV and MIFV curves were recorded at the mouth with a Lilly-type pneumotachograph and integrator. The airway resistance (Raw) was measured at functional residual capacity (FRC) in a constant-volume plethysmograph (Jaeger, FRG) as the chord slope between inspiratory and expiratory flows at 0.5 $l \cdot s^{-1}$; the specific airway conductance (sGaw) was calculated as the reciprocal of Raw divided by thoracic gas volume. Residual volume (RV) and total lung capacity (TLC) were measured by body plethysmography (Jaeger, FRG). The lung function tests were carried out according to the European Respiratory Society (ERS) recommendations [21, 22] and were expressed in absolute values and as a percentage of the reference values of the European Community for Coal and Steel (ECCS) [21], except for Raw and specific airway conductance (sGaw), which were expressed as a percentage of the reference values of AMREIN *et al.* [23].

Radiological data were obtained by CT-scan (General Electric 8800, USA) and by X-ray of the trachea, both at resting end expiratory volume and were analysed by the research team (RP and JV). CT-measurements were made with the patient in supine position; scans were obtained at 10 mm intervals from the level of the mandibula to the carina, with a 5.76 s scanning time. Transverse diameters were measured in two perpendicular directions (coronal and sagittal), and cross-sectional areas were measured with the help of the software programme of General Electric (ROI). Minimal cross-sectional area (CT_1) at the level of the obstruction was compared with the cross-sectional area 2 cm above the carina (CT_2), which was used as reference. From these values the ratio of CT_1 to CT_2 ($CT_{1/2}$) was calculated.

X-rays of the trachea were made in standing subjects in anteroposterior and lateral position. From these, transverse diameters in coronal and sagittal plane were measured at the level of the obstruction; the mean of both diameters was called X-dia$_1$. Maximal transverse diameters in both planes were measured 2 cm above the carina. When this level was not well-visualized, then the maximal diameters were measured at a level where the tracheal diameter remained the same over at least 2 cm; the mean of both diameters was called maximal transverse diameter (X-dia$_2$). The ratio X-dia$_1$ to X-dai$_2$ was calculated (X-dia$_{1/2}$). Also the tracheal cross-sectional areas were calculated at both levels (min=X-area$_1$; max=X-area$_2$) assuming an elliptical shape. The percentage reduction in cross-sectional area (X-area$_{1/2}$) was calculated. A magnification factor of 1.25 was used for the dimensional amplification. The reasons for using the tracheal dimensions at 2 cm above the carina as a reference were: 1) reference values of healthy control subjects are unreliable because interindividual differences are large (at least 50%) and not clearly related to anthropometric data [10–19]; and 2) the intra-individual variations between transverse dimensions at different levels of the trachea are quite small. Although the tracheal diameters at the level 2 cm above the carina are about 10% greater than in the middle part, this relationship is highly reproducible between subjects [24, 25].

Statistics

Means±1 SD were calculated. Correlation coefficients were obtained by the least square method and linear regressions were calculated and evaluated by Student's t-tests. Analyses of variance were applied, and a Duncan test was carried out to determine the significance of differences between the three subgroups. The level of significance was set at $p<0.05$.

Table 1. – Anthropometric data and lung function indices (n=28 females)

	mean	%pred
Age yrs	68±13	
Weight kg	67±17	
Length cm	162±6	
VC l	2.6±0.7	97±19
TLC l	4.8±0.8	97±14
FEV_1 l	1.7±0.6	82±23
FIV_1 l	2.0±0.7	99±24
PEF $l \cdot s^{-1}$	3.6±1.3	62±21
MEF_{50} $l \cdot s^{-1}$	1.9±0.8	56±21
MIF_{50} $l \cdot s^{-1}$	2.1±0.9	57±24
Raw $kPa \cdot l^{-1} \cdot s$	0.38±0.14	149±58
Gaw $l \cdot kPa^{-1} \cdot s^{-1}$	3.1±1.0	
sGaw $kPa^{-1} \cdot s^{-1}$	1.0±0.3	70±24
MEF_{50}/MIF_{50} $l \cdot s^{-1}/l \cdot s^{-1}$	1.0±0.6	
%/%	1.1±0.6	
PEF/MEF_{50} $l \cdot s^{-1}/l \cdot s^{-1}$	2.0±0.8	
%/%	1.2±0.5	
FEV_1/PEF $ml/l \cdot min^{-1}$	8.2±1.8	
%%	1.4±0.3	
MEF_{50}/Gaw $l \cdot s^{-1}/kPa^{-1} \cdot l \cdot s^{-1}$	0.7±0.3	
$\%/kPa^{-1} \cdot l \cdot s^{-1}$	20.3±7.1	

Data are presented as mean±SD. VC: vital capacity; TLC: total lung capacity; FEV_1: forced expiratory volume in one second; FIV_1: inspiratory volume in one second; PEF; peak expiratory flow; MEF_{50} and MIF_{50}: maximal expiratory and inspiratory flows at 50% VC; Raw: airway resistance; Gaw: airway conductance; sGaw: specific airway conductance. Predicted values are from [21] and [22]. For the ratios the same units are used as in MELISSANT *et al.* [5].

Table 2. – Computer tomography (CT)-scan and X-ray data

		n
CT-scan		
Diameters		
Min. sagittal cm	1.25±0.19	26
coronal cm	0.85±0.20	26
Max. sagittal cm	1.70±0.27	26
coronal cm	1.46±0.36	26
Cross-sectional areas		
Min. (CT_1) cm^2	1.4±0.4	26
Max. (CT_2) cm^2	2.4±0.6	26
Ratio ($CT_{1/2}$) %	58±17	26
X-ray		
Diameters		
Min. sagittal cm	1.15±0.33	17
coronal cm	0.93±0.35	22
mean (X-dia_1) cm	0.96±0.32	16
Max. sagittal cm	1.73±0.34	17
coronal cm	1.64±0.37	22
mean (X-dia_2) cm	1.70±0.40	16
Ratio sagittal %	67±15	17
coronal %	58±22	22
mean X-$dia_{1/2}$ %	60±17	16
Cross-sectional areas		
Min. (X-$area_1$) cm^2	0.91±0.5	51
Max. (X-$area_2$) cm^2	2.42±0.93	16
Ratio (X-$area_{1/2}$) %	39±23	16

Minimal (Min.) diameters and cross-sectional areas were measured at the level of the obstruction. Maximal (Max.) diameters and cross-sectional areas were measured 2 cm above the carina (or alternatively for the X-ray at a level close to it where tracheal size did not change over a length of 2 cm). Coronal: laterolateral; sagittal: anteroposterior.

Table 3. – Correlation coefficients between various lung function indices

	FEV_1	PEF	MEF_{50}	FIV_1	MIF_{50}	Raw
PEF	0.73*	-	-	-	-	-
MEF_{50}	0.77*	0.57†	-	-	-	-
FIV_1	0.65†	0.71*	0.38	-	-	-
MIF_{50}	0.63*	0.56†	0.39†	0.53†	-	-
Raw	-0.58†	-0.33	-0.49†	-0.52†	-0.53†	-
sGaw	0.64†	0.24	0.62†	0.25	0.32	0.81*

For abbreviations see legend to table 1. Values are in % predicted, yet results are very similar when absolute values are used. †: $p<0.05$; *: $p<0.01$.

Results

The anthropometric and lung function data of the total group are given in table 1. The changes in the dynamic expiratory and inspiratory indices are not uniform: peak expiratory flow (PEF), MEF_{50} and MIF_{50} are reduced to about 60% of the predicted values, whereas FEV_1 and, in particular FIV_1 are still within normal limits. Static lung volumes are normal, as can be expected. The values of the ratios of some dynamic lung function indices (MEF_{50}/MIF_{50}, FEV_1/PEF, PEF/MEF_{50}, MEF_{50}/Gaw) fall within the ranges expected in UAO [5, 8, 9].

The radiological data are depicted in table 2. On CT-scan, the minimal tracheal lumen is 58±17% of the "reference" (or maximal) cross-sectional area; on X-ray the minimal diameter is 60±17% of the "reference" diameter, but the ratio of the calculated cross-sectional areas

Table 4. – Anthropometric and radiological data in the three UAQ subgroups: variable extrathoracic (E), fixed (F) and variable intrathoracic (I)

	E	F	I	Duncan test
Patients n	6	11	11	
Age yrs	59±12	70±12	71±14	EFI
Weight kg	80.8±24.8	62.2±7.9	64.2±12.7	E-FI
Length cm	163.0±7.2	161.9±4.7	160.3±7.6	EFI
MEF_{50}/MIF_{50} $l \cdot s^{-1}/l \cdot s^{-1}$	1.9±0.6	1.0±0.1	0.6±0.2	E-F-I
TLC % pred	88.6±14.5	97.3±11.9	109.0±5.3	EF-FI
FEV_1 % pred	72.7±19.7	88.4±21.1	80.5±26.4	EFI
FIV_1 % pred	86.2±19.4	97.9±27.2	103.4±22.1	EFI
PEF % pred	53.3±22.7	63.6±22.2	64.6±18.7	EFI
MEF_{50} % pred	51.9±21.7	67.9±19.6	45.7±18.1	EF-FI
MIF_{50} % pred	27.4±10.7	57.9±17.4	71.9±20.6	E-FI
Raw $kPa \cdot l^{-1} \cdot s$	0.48±0.20	0.33±0.10	0.32±0.10	EF-FI
sGaw $kPa^{-1} \cdot s^{-1}$	1.0±0.5	1.1±0.3	1.0±0.3	EFI
PEF/MEF_{50}				
%/%	1.1±0.4	0.9±0.3	1.6±0.6	EF-I
$l \cdot s^{-1}/l \cdot s^{-1}$	1.8±0.6	1.6±0.4	2.7±1.0	EF-I
FEV_1/PEF				
%/%	1.5±0.3	1.5±0.3	1.3±0.4	EFI
$ml/l \cdot min^{-1}$	9.5±2.7	8.5±1.2	7.2±1.7	EF-FI
MEF_{50}/Gaw				
$\%/kPa^{-1} \cdot l \cdot s^{-1}$	22.7±7.0	21.9±8.4	15.8±4.0	EFI
$l \cdot s^{-1}/kPa^{-1} \cdot l \cdot s^{-1}$	0.9±0.3	0.8±0.3	0.6±0.1	EFI
CT_1 cm^2	1.4±0.3	1.3±0.3	1.5±0.5	EFI
CT_2 cm^2	2.7±0.6	2.5±0.6	2.3±0.6	EFI
$CT_{1/2}$ %	54±14	54±16	64±19	EFI
X-dia_1 cm	1.0±0.5	0.9±0.5	1.1±0.3	EFI
X-dia_2 cm	1.8±0.5	1.7±0.6	1.6±0.4	EFI
X-$dia_{1/2}$ %	55±23	50±13	70±13	EFI

Data are presented as mean±SD. For abbreviations see legend to table 1. Groups separated by dash in Duncan test differ significantly ($p<0.05$).

is only 39±23%. The length of the obstruction on X-ray is 4.3±1.5 cm.

In table 3, the correlations between the lung function indices are presented. As could be expected, most lung function indices are significantly correlated to each other.

For the radiological data, no significant correlations are found with the anthropometric data except between X-dia$_2$ (maximal diameter) and body height ($r=0.51$; $p<0.05$). Also, between X-ray and CT-scan significant correlations are only found between X-dia$_2$ and CT_2 ($r=0.54$, $p<0.05$) and between X-dia$_{1/2}$ and $CT_{1/2}$ ($r=0.50$, $p<0.05$).

The correlations between the lung function indices and the radiologic parameters are not significant, except between CT_2 and Raw or sGaw ($r=0.51$ and $r=0.60$ respectively; $p<0.05$).

Table 4 presents the data obtained by subdividing the patients into three subgroups (variable extrathoracic obstruction; fixed obstruction; and variable intrathoracic obstruction) based on the MEF_{50}/MIF_{50} ratio. Variable extrathoracic obstruction is significantly different from both other groups for weight and MIF_{50}; it is different from variable intrathoracic obstruction for TLC, MEF_{50}, Raw and FEV_1/PEF. Variable intrathoracic obstruction is different from the two other groups for PEF/MEF_{50}. The lung function abnormalities tend to be most pronounced in variable extrathoracic obstruction and least pronounced in variable intrathoracic obstruction. No differences are found between the three subgroups for the CT-scan and X-ray indices, although the minimal diameters, the minimal cross-sectional areas and the ratios tend to be larger in variable intrathoracic obstruction.

Discussion

The main purpose of this study was to search for simple but clinically useful and relevant functional and radiologic indices, which reliably reflect the degree of tracheal narrowing in UAO. Furthermore, we were interested in the correlation between changes in lung function indices (measured during large manoeuvres and during quiet breathing) and changes in radiological dimensions of the trachea (cross-sectional area and transverse diameters measured by CT-scan and X-ray) in UAO.

We, therefore, studied 28 female patients with UAO due to thyroid goitre. The findings were that pulmonary function tests showed a reduction in maximal flows (PEF, MEF_{50}, MIF_{50}) to about 60% predicted, and in sGaw to 70% predicted; the radiologic evaluation showed a reduction in cross-sectional area on CT-scan and in transverse diameters of the trachea on X-ray to about 60%. Whilst most lung function data were significantly correlated with each other, this was not the case for the radiological changes at the level of the UAO. In addition, no correlation was found between the abnormalities in pulmonary function tests and in radiological dimensions.

Some methodological and technical aspects of the study need an explanation. Firstly, lung function changes were related to the reference values of healthy control populations [21–23], whilst the radiological changes were related to a reference area in the trachea of each subject. The reason for this is that tracheal transverse dimensions, in contrast to lung function data, are not well-correlated with anthropometric data, such as age, sex and height, and in addition show wide interindividual variations (of more than 50% despite comparable anthropometric characteristics) [10–19]. Therefore, expressing changes of tracheal dimensions in percentage of the values in a control population is not useful. Studies comparing airway size with lung or body size have, indeed, not yielded consistent results and several of these studies were unable to find any significant correlation [10–19]. The latter was attributed to dysanapsis *i.e.* the apparently unequal growth pattern of the tracheobronchial tree and the lung parenchyma [12]. On the other hand, the transverse dimensions at different levels of the trachea vary less than 10% from each other, except at the glottis and the carina *e.g.* the difference between the level at 2 cm above the carina and the middle part of the trachea is 10% at the most [24, 25]. Since, in our patients, the trachea at the level of 2 cm above the carina was always at a distance from the narrowed area and was well-visualized in most subjects, it was used as reference zone. The tracheal dimensions measured by CT-scan and X-ray in our study were grossly comparable with the data from the literature [10, 13–16, 19], although Brooks *et al.* [10] obtained somewhat smaller values. In agreement with most of these studies, we found no significant correlation between the normal tracheal dimensions (in our study measured at the unaffected level 2 cm above the carina) and the anthropometric data (such as height and age) or the lung volumes (such as spirometry or maximal flows, expressed in absolute values). There was, however, a significant correlation between the tracheal cross-sectional area at 2 cm above the carina (CT_2) and Raw.

Secondly, it was our purpose to use radiological and lung function methods that are routine techniques. Indeed, spirometry with maximal flow volume curves, body plethysmography, CT-scan and X-rays are readily available in a clinical set-up.

Among the lung function indices obtained during forced manoeuvres, the maximal flow-volume loops, in particular, were very informative to characterize the UAO [5, 20] and to categorize it into several subgroups (fixed, variable extrathoracic, or variable intrathoracic). Several ratios (*i.e.*PEF/MEF_{50}<2.1 %/% or FEV_1/PEF >8 $ml/l{\cdot}min^{-1}$) used to differentiate UAO from COPD and asthma [8, 9, 26, 27] were also indicative of UAO in our patients. In addition, the MEF_{50}/Gaw (*i.e.* the ratio of the airway patency during a forced expiration to that during quiet breathing) was increased to 20.3±7.1 $\%/kPa^{-1}{\cdot}l{\cdot}s^{-1}$ or 0.7±0.3 $l{\cdot}s^{-1}/kPa^{-1}{\cdot}l{\cdot}s^{-1}$ which we have previously shown to be an index of UAO [5]. Although the maximal flow-volume indices and the derived ratios are very sensitive for describing UAO, and although most lung function tests are significantly correlated with each other, it remains to be determined which is the best lung function test to reflect the degree of UAO or the severity of the functional impairment in UAO. FEV_1 is known to give a gross underestimation. PEF is probably less accurate due to its effort dependence. MEF_{50} and MIF_{50} are apparently reliable reflections of the airway narrowing during the forced manoeuvre, but this may differ from the situation during quiet breathing, due to dynamic compression or collapse of the airways. Measurements during quiet breathing are probably more relevant as a reflection of the functional impairment during daily life, and, therefore, we propose that Raw, Gaw or sGaw might be the most appropriate tests. Indeed, several studies have shown that among the lung function tests, airway resistance is best correlated with tracheal dimensions in healthy women [10, 17]. In our study airway resistance was the only pulmonary function test which was significantly correlated with a radiologic index; however, not at the narrowed level of the trachea but at the level 2 cm above the carina. Clearly, further studies are needed to determine the clinically most relevant pulmonary function test.

Concerning the comparison between the two radiological techniques, only the correlation between the tracheal narrowing measured with CT-scan ($CT_{1/2}$) and X-ray (X-$dia_{1/2}$) was significant. One could speculate that the fact that X-ray is done in upright posture and CT-scan in supine posture may be an explanation for the poor correlation between the two techniques. The CT-scan allowed the tracheal cross-sectional area to be measured at the level of the UAO in 26 of the 28 subjects, whilst the X-ray was evaluable in only 16 subjects. For this reason, CT-scan seems to be more appropriate than X-ray to evaluate the degree of UAO. It should be noted that the percentage narrowing was quite different between the two methods: the cross-sectional area at the level of the UAO estimated from the X-ray was 39% of the reference area, whilst the CT-scan measured a value of 58%, which is more in agreement with the value of about 60% predicted obtained with the lung function tests.

The correlations between most lung function indices and the radiological measurements were weak. There are several explanations for this. With the exception of Raw (and implicitly Gaw and sGaw), the dynamic lung function indices were measured during large, forced manoeuvres. Furthermore, the radiological measurements were made at resting end-expiratory volume, whereas the trajectory of the large dynamic manoeuvres included the whole VC. It is known that the diameter of the tracheal lumen varies with the phase of respiration and with lung volume, being largest at TLC and smallest at RV [19]. Finally, the geometrically complex structure of the upper airways is subject to considerable variability with changes in position [28]. In this study, lung function variables and tracheal X-rays were obtained with the patient in upright sitting position whereas for the CT-scan the patient was supine.

In conclusion, this study shows that routinely available radiographic methods did not offer a significant contribution to the evaluation of the impairment in patients with UAO. We agree with Shepard *et al.* [29], that future studies on anatomical, pathological and functional relationships in UAO should preferably consider the simultaneous measurement of lung function and radiological imaging. Fast CT-scanning gives a clear dynamic imaging in transverse orientation and includes very transient phenomena [30]. Nevertheless, at present, this type of CT-scan is not widely available, so that, in general, its value remains experimental rather than routine. Also, the acoustic reflection technique might give more insight in the pathophysiological changes in UAO [10, 19, 31, 32]. Meanwhile, we can only conclude that in our group of patients with a goitre, both routine lung function tests and CT-scan depict the UAO although both techniques are not well correlated to each other. X-ray of the trachea would not visualize the obstruction in almost half of the subjects and is, therefore, not reliable.

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