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Total effective time of the forced expirogram in disease: sources of error and a correction factor

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ABSTRACT Effective time of the forced expirogram is a sensitive index for the detection of mild airways obstruction. However, there is evidence that this measurement is not superior to maximum flow rates in the lower half of the forced vital capacity or even FEV_1 and $FEV_1\%$ in some patients suffering from obstructive lung disease. Furthermore we noticed that in some patients with a decrease of the forced vital capacity caused by exacerbation of airways obstruction, the effective time was not appreciably changed. We concluded that this apparent diasdvantage of the effective time is the result of the different forced vital capacities. To eliminate this error we transformed the forced expirogram to the equivalent curve that the patient would produce, if his forced vital capacity was equal to the predicted mean value for his age, sex, and height. The derived corrected total effective time seems to have increased sensitivity for detection of small changes in expirograms obtained from the same subject or from different subjects.

It has been shown that the total effective time ($teff_T$) or its equal mean transit time (MTT) of the forced expiratory spirogram (FVC-t curve) is a sensitive parameter for the detection of upper and lower airways obstruction.[1-4] However, we noticed that in patients with obstructive lung disease the total effective time was not so long as expected. Bello *et al*[5] found that bronchodilatation was better assessed with FEV_1 and $\dot{V}_{50}$ than with MTT and the other moments. Osmanliev *et al*[6] found that MTT was no better than $\dot{V}_{50}$, $\dot{V}_{25}$ in separating smokers from non-smokers. Moreover, Liang *et al*[7] noticed that MTT was not more sensitive than MMEF, $\dot{V}_{25}$, $\dot{V}_{50}$, $FEV_1\%$ in detecting change after inhalation of salbutamol aerosol. These findings represent a considerable disadvantage of this parameter ($teff_T$, MTT) in the assessment of airways obstruction.

Methods

We studied 25 patients, of whom seven had chronic bronchitis, eight bronchial asthma, one tracheal stenosis caused by carcinoma, and nine lung fibrosis. The diagnosis of the disease was made on clinical and radiological grounds. The functional abnormality was assessed mainly by simple spirometry (FVC, FEV_1, $FEV_1\%$, $teff_T$). Open lung biopsy in patients with fibrosis was performed in five patients and skin biopsy in one. Bronchoscopy was performed in the patient with tracheal stenosis.

The lung function tests were performed in most of the patients before and on several occasions during treatment. The patient in the sitting position expired maximally from total lung capacity (TLC) to residual volume (RV) through a mouthpiece (id 2·55 cm) into a water spirometer. The speed of the paper was 20 mm/s.

Great care was taken to ensure that the patient expired as forcibly as possible and until no further air could be expelled. Three maximal expirograms were recorded with a time interval of five minutes between the expiratory manoeuvres. The curve with the maximum FVC was selected for the calculation of FVC, FEV_1, $FEV_1\%$, and effective time (teff). Effective time was calculated in the complete expirogram (total effective time, $teff_T$) and in the part of the curve corresponding to the time interval of six seconds ($teff_6$). We also calculated the corrected total effective time ($teff_{TC}$), using the equation.

$$teff_{TC} = teff_T \,/\, \frac{FVC}{FVC_N}$$

(see Appendix)
(Where: FVC = actual value of the patient's FVC and FVC_N = predicted normal value of the FVC for the patient.)[8]

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Table 1 *Measurements from five patients in whom FVC/predicted FVC was ⩾ 1. Numbers in brackets indicate the normal range for the ratios*

Disease	*FVC/FVC*$_N$	*FEV*$_1$*%/FEV*$_1$*%N*	$teff_T/teff_{TN}$	$teff_{TC}/teff_{TN}$
Chronic bronchitis	0·98	0·94	1·18	1·18
	1·00	0·87	1·43	1·43
	1·06	0·84	1·82	1·72
	(0·9-1·1)		(0·75-1·25)	
Asthma	1·12	1·04	1·75	1·57
	1·16	1·00	2·05	1·77
	(0·9-1·1)		(0·88-1·12)	
Asthma	1·08	1·03	1·12	1·04
	(0·9-1·1)		(0·77-1·23)	
Asthma	1·19	0·81	1·61	1·35
	1·12	0·72	2·23	2·01
	1·07	0·59	2·88	2·70
	(0·9-1·1)		(0·77-1·23)	
Asthma	1·00	0·99	1·56	1·56
	(0·9-1·1)		(0·88-1·12)	

Table 2 *Measurements from five patients with long* $teff_{TC}$ *and normal* $teff_T$*. Numbers in brackets indicate the normal range for the ratios*

Disease	*FVC/FVC*$_N$	*FEV*$_1$*%/FEV*$_1$*%N*	$teff_T/teff_{TN}$	$teff_{TC}/teff_{TN}$
Chronic bronchitis	0·68	0·96	1·07	1·58
	(0·9-1·1)		(0·75-1·25)	
Fibrosis	0·63	1·03	0·90	1·42
	0·76	1·09	1·10	1·44
	(0·9-1·1)		(0·88-1·12)	
Fibrosis	0·54	1·12	0·84	1·58
	(0·9-1·1)		(0·75-1·25)	
Fibrosis	0·51	1·05	0·75	1·48
	(0·9-1·1)		(0·75-1·25)	
Fibrosis	0·71	1·02	0·91	1·30
	(0·9-1·1)		(0·88-1·12)	

Results

Seventy maximal expirograms obtained from 25 patients were studied. The results are expressed as the ratio of the patient's value for $teff_T$, $teff_{TC}$, FVC and FEV_1% over the corresponding predicted mean value. In all the patients $teff_{TC}$ was longer than $teff_T$, except in 10 curves from five obstructive patients in which the ratio FVC/FVC_N was greater than or equal to unity (table 1). In six curves from five patients $teff_{TC}$ was abnormally long while $teff_T$ was normal (table 2). In 21 curves from nine patients suffering from airways obstruction and fibrosis worsening of the clinical condition was associated with no change or even shortening of $teff_T$ while $teff_{TC}$ was becoming longer (table 3).

The reduction of the FEV_1% ratio was followed by the elongation of $teff_{TC}$. However in 33 expirograms from 15 patients suffering from airways obstruction and fibrosis deterioration of the clinical condition was associated with a small change (<5%) (decrease or even an increase) of the FEV_1% ratio while $teff_{TC}$ was becoming longer (table 4). In these patients the $teff_T$ did not always follow the change of $teff_{TC}$. The effective time measured at the time interval of six seconds ($teff_6$) was compared to the total effective time ($teff_T$) in 38 expirograms from 16 patients suffering from chronic bronchitis and

Table 3 *Measurements from nine patients in whom* $teff_{TC}$ *lengthened but* $teff_T$ *did not when condition deteriorated. Numbers in brackets indicate the normal range for the ratios. Worsening of the clinical condition is according to the direction from above downwards for each patient*

Disease	*FVC/FVC*$_N$	$teff_T/teff_{TN}$	$teff_{TC}/teff_{TN}$
Chronic bronchitis	0·95	1·98	2·08
	0·79	1·74	2·20
	(0·9-1·1)	(0·77-1·23)	
Chronic bronchitis	0·51	2·17	4·28
	0·45	2·15	4·82
	0·38	2·17	5·79
	(0·9-1·1)	(0·77-1·23)	
Tracheal stenosis	0·75	2·59	3·47
	0·75	3·26	4·38
	0·30	1·71	5·59
	(0·9-1·1)	(0·75-1·25)	
Asthma	0·96	1·67	1·74
	0·92	1·62	1·77
	0·60	1·47	2·46
	(0·9-1·1)	(0·77-1·23)	
Asthma	1·12	1·75	1·57
	0·38	1·30	3·44
	(0·9-1·1)	(0·88-1·12)	
Asthma	1·07	2·88	2·70
	0·60	2·16	3·59
	(0·9-1·1)	(0·77-1·23)	
Asthma	0·57	3·47	6·09
	0·47	3·34	7·09
	(0·9-1·1)	(0·75-1·25)	
Asthma	0·87	2·60	2·98
	0·72	2·60	3·58
	(0·9-1·1)	(0·75-1·25)	
Fibrosis	0·64	0·30	0·47
	0·45	0·30	0·67
	(0·9-1·1)	(0·75-1·25)	

Table 4 *Measurements from 15 patients in whom teff$_{TC}$ lengthened but FEV$_1$%/predicted FEV$_1$% changed little when condition worsened. Clinical deterioration is from above downwards for each patient*

Disease	*FVC/FVC$_N$*	*FEV$_1$%/FEV$_1$%N*	*teff$_{TC}$/teff$_{TN}$*
Chronic bronchitis	0·60	0·74	3·32
	0·62	0·73	3·56
Chronic bronchitis	0·95	0·76	2·08
	0·79	0·82	2·20
Chronic bronchitis	0·72	0·71	1·95
	0·72	0·72	2·68
Chronic bronchitis	1·00	0·87	1·43
	1·06	0·84	1·72
Chronic bronchitis	0·32	0·46	8·41
	0·42	0·41	8·79
Chronic bronchitis	0·51	0·66	4·28
	0·45	0·66	4·82
	0·38	0·66	5·79
Tracheal stenosis	0·75	0·55	3·47
	0·75	0·50	4·38
	0·30	0·65	5·59
Asthma	0·92	0·92	1·77
	0·60	0·94	2·46
Asthma	1·12	1·04	1·57
	1·16	1·00	1·77
Asthma	0·96	0·95	1·35
	0·95	0·94	1·50
	0·91	0·95	1·70
Asthma	1·07	0·59	2·70
	0·60	0·60	3·59
Asthma	0·80	0·75	3·46
	0·72	0·77	3·58
Asthma	0·93	0·99	1·36
	1·00	0·99	1·56
Fibrosis	0·76	1·09	1·44
	0·69	1·06	1·78
Fibrosis	0·64	1·35	0·54
	0·45	1·38	0·67

bronchial asthma. Eleven of these patients in 22 expirograms showed teff$_6$ definitely shorter than teff$_T$.

Discussion

Total effective time (teff$_T$) was originally developed from a single exponential volume-time curve and then applied to multiple exponential curves.[4] The ratio of the area ($\int Vdt$) to the volume change (V) was called effective time (teff) because it was shown in volume-time curves, mainly inspiratory, during spontaneous breathing, that the ratio V/2 teff was equal to the effective value of flow (root mean square flow) (unpublished data). Mean transit time of the maximal expirogram (MTT) is the first statistical moment of the curve.[1-3 9-11] These two terms (teff$_T$, MTT) have the same value if measured at the same time interval on the expirogram.

In normal young subjects as well as in patients suffering from fibrosis there is no difference between teff$_T$ and teff$_6$ because forced expiratory time (FET) is shorter than six seconds. However, in patients with airways obstruction, in whom FET is longer than six seconds, teff$_T$ is longer than teff$_6$. According to the above, the six seconds time interval used for the calculation of teff$_6$ reduces the sensitivity of this parameter. It may be argued that the duration of the FVC is as arbitrary as using a fixed interval, say of six seconds. The whole FVC-t curve is the result of the maximum effort of the patient and the duration time of three consecutive expirograms may be different. The maximum value of the FVC in one of these expirograms does not necessarily imply that its forced expiratory time will also be the maximal. Small changes in FET in consecutive expirograms from the same subject do not affect materially the magnitude of the effective time (unpublished data).

It has been suggested that mathematical extrapolation to infinity of the FVC-t curve would avoid the difficulty in selecting the end-point for the calculation of teff. This method could be applied if the maximal expirogram followed a certain mathematical expression. We have found that the majority of the expirograms are multiple exponential curves (unpublished data). So the extrapolation curve to infinity between the point of the patient's RV and that of the patient's normal value of RV cannot be predicted.

It has been noticed in some patients with a considerable decrease in FVC that the total effective time is normal or deviates slightly from normality while other parameters (FVC, FEV$_1$, FEV$_1$%) and the clinical findings indicate airways obstruction. In order to overcome this apparent disadvantage of teff$_T$ we transformed the actual FVC-t curve to the equivalent curve that the patient with the same mechanical condition of the "lung-chest wall" would produce if his FVC was equal to the predicted mean value for his age, sex and height. The transformation of the FVC-t curve to the equivalent curve is based on the following concept: two maximal expirograms with different FVC are compared to each other in terms of volume change at several preselected time intervals which are the same for both expirograms. It is evident that, when the comparison is to be made in terms of time, the preselected volumes must also be the same. The actual FVC-t curve and its equivalent curve have the same mean flow (see Appendix). By using this concept we actually compare in terms of time the equivalent FVC-t curves of patients with the same predicted normal FVC values. The transformation of the actual FVC-t curve was achieved by dividing the coordinates of each point along the curve by the factor FVC/FVC$_N$. The effective time of the equivalent curve was called corrected total effective time (teff$_{TC}$) (Appendix). In this way it was possible to relate properly to each other, in terms of effective time, expirograms with different vital capacities obtained from the same subject or from different subjects with the same predicted normal

FVC values. There may be an argument that in the case of lung resection the corrected total effective time will give an incorrect image of the situation. The total effective time of the expirogram obtained from a normal subject is the same as that obtained from one lung only and each lung has the same $teff_T$ as that of the contralateral lung (unpublished data). In a patient with one lung excised and the other lung normal $teff_T$ is normal while $teff_{TC}$ is nearly doubled because $FVC/FVC_N \simeq 0{\cdot}5$. In this particular case the ratio $FVC_N/2\ teff_{TC}$ is equal to $FVC/2\ teff_T$, which is nearly the same with the mean flow ($\Sigma_{t_0}^{t}\ \dot{V}/t$) obtained from a flow-time curve. The differential diagnosis of prolonged $teff_{TC}$ between excised lung and airways obstruction can be made by using the static lung capacity TLC and the ratio RV/TLC. Patients with chronic bronchitis or bronchial asthma during treatment showed no appreciable further change in FVC, FEV_1, $FEV_1\%$ and $teff_T$ while $teff_{TC}$ was improving. This is the result of a small increase in FVC; decrease in $teff_T$, which alone is not of any practical importance, resulted in a definite reduction of $teff_{TC}$. This may be of particular interest in clinical medicine as it implies that, even if maximum improvement of the parameters FVC, FEV_1, $FEV_1\%$, and $teff_T$ is achieved, treatment has to be continued until $teff_{TC}$ can be shortened no further. The fact that FVC, FEV_1, $FEV_1\%$, and/or $teff_T$ remain practically stable while $teff_{TC}$ improves may be considered as evidence that this is a sensitive method for assessing the mechanical performance of the "chest wall-lung" system.

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Appendix

The mechanical behaviour of the "chest wall-lung" system is reflected in the morphology of the maximal expirogram. The curvature of the FVC-t curve, at any point along it, expresses the relationship between volume change and time, ie, the instantaneous flow, and it can be defined by its coordinates on the volume and time axes. By dividing each of these coordinates by the ratio FVC/FVC_N the real FVC-t curve is extended to the equivalent curve without changing the value of the instantaneous flow at that point (figure). So the patient's expirogram is transformed to the equivalent curve with FVC equal to the predicted normal mean value for his age, sex and height and in which the mean expiratory flow ($FVC_N/2\ teff_{TC}$) is equal to that of the real curve ($FVC/2\ teff_T$). The relationship between $teff_T$, FVC/FVC_N and $teff_{TC}$ is given by the equation.

$$teff_{TC} = teff_T \Big/ \frac{FVC}{FVC_N}$$

In the figure the real maximal expirogram of an obstructive patient (.-.-.) is transformed to the equivalent curve (o-o-o) by dividing each of the volume and time coordinates at any point along the real curve by the ratio FVC/FVC_N. The angles a and b are equal to each other and their tangent represents the mean expiratory flow.

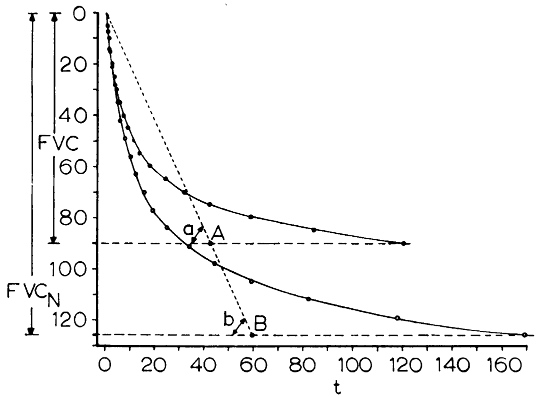

Figure *Real maximal expirogram (above) of an obstructive patient and the equivalent curve (below). The equivalent curve is calculated by dividing the coordinates of each point on the real expirogram by the factor FVC/FVC_N. The ratio of the area $\int \dot{V}dt$ of the equivalent curve over FVC_N is the corrected total effective time ($teff_{TC}$). The relationship between $teff_{TC}$,*

$teff_T$ and FVC/FVC_N is given by the equation

$$teff_{TC} = teff_T \Big/ \frac{FVC}{FVC_N}$$

The point A corresponds to 2 $teff_T$ of the real curve and point B to 2 $teff_{TC}$ of the equivalent curve. Angle a is equal to angle b and the tangent of these angles is the mean expiratory flow which is the same in both curves—ie, $FVC/2\ teff_T = FVC_N/2\ teff_{TC}$. FVC is the real forced vital capacity of the patient and FVC_N is the predicted normal value for his age, height, and sex. Zero point on volume axis corresponds to the level of TLC. Volume and time axis in millimetres (1 mm = 0·03 l, 1 mm = 0·05 s). In this example, FVC/FVC_N = 0·715, $teff_T$ = 1·066 s (predicted: 1·121 s), $teff_{TC}$ = 1·491 s, $FVC/2\ teff_T = FVC_N/2\ teff_{TC}$ = 1·266 l/s).