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Use of tidal breathing curves for evaluating expiratory airway obstruction in infants

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ABSTRACT

Objective: To evaluate tidal breathing (TB) flow-volume and flow-time curves for identification of expiratory airway obstruction in infants. **Methods:** Pulmonary function tests were analyzed retrospectively in 156 infants aged 3–24 months with persistent or recurrent respiratory complaints. Parameters derived from TB curves were compared to maximal expiratory flow at functional residual capacity ($\dot{V}_{\text{maxFRC}}$) measured by rapid thoracoabdominal compression technique. Analyzed parameters were: inspiratory time (t_i), expiratory time (t_E), tidal volume, peak tidal expiratory flow (PTEF), time to peak tidal expiratory flow (t_{PTEF}), expiratory flow when 50% and 25% of tidal volume remains in the lungs (FEF_{50} , FEF_{25} , respectively), and the ratios t_{PTEF}/t_E , t_i/t_E , $\text{FEF}_{50}/\text{PTEF}$, and $\text{FEF}_{25}/\text{PTEF}$. Statistical comparisons between flow indices and TB parameters were performed using mean squared error and Pearson's sample correlation coefficient. The study population was also divided into two groups based on severity of expiratory obstruction (above or below z-score for $\dot{V}_{\text{maxFRC}}$ of -2) to generate receiver operating characteristic (ROC) curves and calculate discriminatory values between the groups. **Results:** TB parameters that were best correlated to $\dot{V}_{\text{maxFRC}}$ were: t_{PTEF}/t_E , $\text{FEF}_{50}/\text{PTEF}$, and $\text{FEF}_{25}/\text{PTEF}$, with $r = 0.61, 0.67, 0.65$, respectively ($p < 0.0001$ for all). ROC curves for $\text{FEF}_{50}/\text{PTEF}$, $\text{FEF}_{25}/\text{PTEF}$ and t_{PTEF}/t_E showed areas under the curve of 0.813, 0.797, and 0.796, respectively. Cutoff value z-scores of $-0.35, -0.34$, and -0.43 for these three parameters, respectively, showed an 86% negative predictive value for severe airway obstructions. **Conclusion:** TB curves can assist in ruling out severe expiratory airway obstruction in infants.

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Wheezy infants; infant pulmonary function tests (iPFT); rapid thoracoabdominal compression technique; $\dot{V}_{\text{maxFRC}}$; time to peak tidal expiratory flow (t_{PTEF})

Introduction

Spirometry testing is widely used to measure expiratory air flow in older children and adults. Evaluating airway obstruction in infants is more complicated due to lack of patient cooperation. Instead of spirometry testing, rapid thoracoabdominal compression techniques by means of an inflatable jacket are used to generate forced expiration during infant pulmonary function testing (iPFT) (1). However, these tests are not widely implemented because they are expensive, complicated, and involve sedation. Tidal breathing (TB) flow-volume and flow-time curves recorded during quiet breathing are much less difficult to produce in infants. However, studies have produced conflicting results regarding the ability of certain parameters derived from TB curves to successfully analyze infants with respiratory disease. At our institution, iPFT is routinely performed as part of evaluating infants with respiratory diseases. We retrospectively analyzed several

parameters derived from TB flow-volume and flow-time curves and compared them to the maximal flow at the functional residual capacity ($\dot{V}_{\text{maxFRC}}$). $\dot{V}_{\text{maxFRC}}$ was measured with the tidal forced expiratory flow-volume loops generated using the rapid thoracoabdominal compression technique. Our goals were to determine the pattern of TB in infants with airway obstruction and to evaluate the ability of parameters derived from TB loops to serve as indicators of airway obstruction in infants less than 2 years of age.

Methods

This study is a retrospective analysis of iPFT studies. The infants were referred for PFT by a pediatric pulmonologist as part of their clinical evaluation of persistent or recurrent respiratory complaints. The study was approved by the Ethics Committee of the Hadassah Medical Center.

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Study population

Infants aged 3–24 months who underwent iPFT at Hadasah Medical Center between January 2009 and July 2012 were included in the study. iPFT was not performed during acute state of illness. Infants born before the 34th week of gestation, those with suspected or diagnosed central airway illness, and those with chronic illnesses such as cystic fibrosis, congenital heart disease and interstitial lung disease, were excluded from the study. The reason for excluding infants with chronic diseases other than small airway disease was our hypothesis that TB analysis differs between the two groups. For example, TB curves in infants with upper or central (originating from the trachea or main bronchi) respiratory disease look different than those from infants with small airway problems. We used a relatively homogeneous group to maximize our chances of obtaining significant results.

Infant pulmonary function testing

Measurements were performed according to ATS-ERS guidelines (2–4). Informed consent was given by the children's legal guardians prior to testing. Briefly, the infant was sedated using 100–150 mg/kg triclofos sodium syrup. Flows and volumes were measured using a heated pneumotachograph (series 3700A, Hans Rudolph Inc., USA) connected via a low-dead-space Rendell Baker face mask secured tightly in place with silicone putty. The pneumotachograph was connected to a differential pressure transducer and signal conditioner set to 100 Hz (SCIREQ TD-05 & SC-24). The combined effective dead space of the different mask sizes with the pneumotachograph was 19.5 ml for infants weighing over 9 kg, 17.5 ml for infants weighing between 6 and 9 kg, and 15 ml for infants weighing less than 6 kg (4).

All data acquisition was displayed online in real time during the PFT and quality could thus be immediately assessed and improved. The data were then stored for offline analysis and additional quality assessments and lack of artifacts.

Tidal breathing flow-volume and flow-time curves

Before beginning each recording, we ensured that the infant was breathing calmly and in a relaxed state, and that there was a complete seal around the face mask. Sets of 3–4 tidal breaths were recorded, each containing between 9 and 15 flow-volume loops and flow-time curves (slightly less than those recommended by the ATS-ERS guidelines). The set showing the most reproducible loops was chosen for analysis. Loops with artifacts were discarded.

Measured parameters included: inspiratory time (t_I), expiratory time (t_E), tidal volume, peak tidal expiratory flow (PTEF), time to peak tidal expiratory flow (t_{PTEF}) and expiratory flow when 50% and 25% of tidal volume remains in the lungs (FEF_{50} and FEF_{25} , respectively). TB parameters derived from these measurements included the ratios: t_{PTEF}/t_E , t_I/t_E , $FEF_{50}/PTEF$, and $FEF_{25}/PTEF$.

Maximal expiratory flow at functional residual capacity ($\dot{V}_{maxFRC}$)

$\dot{V}_{maxFRC}$ was assessed using the rapid thoracoabdominal compression technique (giving the tidal forced expiratory flow-volume loop). Several measurements were taken at increasing compression pressures until a target pressure was reached at which the flow at the FRC reached a plateau. Several measurements (between 3 and 7) of $\dot{V}_{maxFRC}$ were taken at the target pressure. The flow-volume loops were evaluated for technical artifacts (such as glottal closure or early interruption of expiration due to braking) and problematic measurements were not included in the final analysis. The highest technically satisfactory value was selected for $\dot{V}_{maxFRC}$ provided that there was at least one other measurement within 10% of this value. We used the regression equations defined by Hoo et al. (5) to define the degree of abnormality on $\dot{V}_{maxFRC}$. The threshold for abnormality and the degree of obstruction were defined using z-scores from the Hoo equations (5).

Statistical analysis

The data from the flow-volume and flow-time curves were analyzed using Matlab 7.0.4. Mean comparisons of iPFT measurements were performed using an unpaired t-test. Statistical comparisons between flow indices and TB parameters were performed using mean squared error and Pearson's sample correlation coefficient. A natural log (ln) transformation for z-score $\dot{V}_{maxFRC}$ was conducted because its distribution was not normal. A logarithmic regression analysis model was performed because it showed the best r^2 relationship.

Study design

Values of the parameters t_{PTEF}/t_E , $FEF_{50}/PTEF$, and $FEF_{25}/PTEF$ were divided into two groups according to the severity of the obstruction demonstrated by $\dot{V}_{maxFRC}$. The logical assumption was that changes in TB curves would be more evident in the infants with more severely obstructed airways since we were not using a forced-exhalation technique. We also wanted

to determine the TB pattern during expiration in severely obstructed infants. Therefore, we initially compared severely obstructed infants (z-score $\dot{V}_{\text{maxFRC}} \leq -2$) to nonobstructed infants (z-score $\dot{V}_{\text{maxFRC}} > -1$). A second comparison was performed to derive a more practical data set. In this comparison, we divided the entire study population into two groups: group I had no to moderate airway obstructions (z-score $\dot{V}_{\text{maxFRC}} > -2$), and group II had severe airway obstructions (z-score $\dot{V}_{\text{maxFRC}} \leq -2$).

A receiver operating characteristic (ROC) curve was then calculated for each group using SPSS (ver. 19). Cutoff values were chosen according to negative predictive values for severe obstruction. The 95% confidence interval of the area under the normalized ROC curve (AUC) was calculated. The accepted level of statistical significance was $p < 0.05$. Cutoff values were standardized using the population means and standard deviations (SD) used to calculate z-scores.

Results

Between January 2008 and December 2012, 320 infants underwent iPFT at our institution. Of these, 156 infants fit the inclusion criteria for the study. Table 1 lists the complaints that generated referral for lung testing. Infants with chronic diseases diagnosed prior to or around the iPFT were excluded.

An average of 12 (range 9–15) TB flow-volume and flow-time curves were analyzed for each infant. The mean SD (in percent) for the three main parameters

Table 1. The various complaints among infants referred to the PFT and were included in this study.

	Number of infants
Persistent/recurrent wheezing	56
Persistent/recurrent cough	85
Post bronchiolitis*	16
Tachypnea	24
Recurrent pneumonia	8

*The test was performed at least one month after the release from hospitalization due to bronchiolitis. Some infants had more than one complaint therefore the sum of the complaints is greater than the total number of infants included in the study.

derived from the analysis— $t_{\text{PTEF}}/t_{\text{E}}$, $\text{FEF}_{50}/\text{PTEF}$ and $\text{FEF}_{25}/\text{PTEF}$ —was 16%, 3.9%, and 7.0%, respectively. Examples of TB flow-volume and flow-time curves and their corresponding tidal expiratory flow-volume loops are shown in Figure 1.

The first comparison was between severely obstructed infants (z-score $\dot{V}_{\text{maxFRC}} \leq -2$) and nonobstructed infants (z-score $\dot{V}_{\text{maxFRC}} > -1$). Results are shown in Table 2. We determined the TB pattern during expiration in obstructed vs. nonobstructed infants. An extended expiration time in the obstructed infants was evidenced by a lower $t_{\text{I}}/t_{\text{E}}$ ($p = 0.01$), while the respiratory rate was similar between the two groups ($p = 0.76$). In addition, there was an earlier t_{PTEF} and lower expiratory flows in the second part of the expiration ($\text{FEF}_{50}/\text{PTEF}$ and $\text{FEF}_{25}/\text{PTEF}$) in the obstructed infants, along with higher peak expiratory and inspiratory flows. Figure 2 gives a graphic demonstration, by way of flow-time curves, of the different breathing patterns between the two groups.

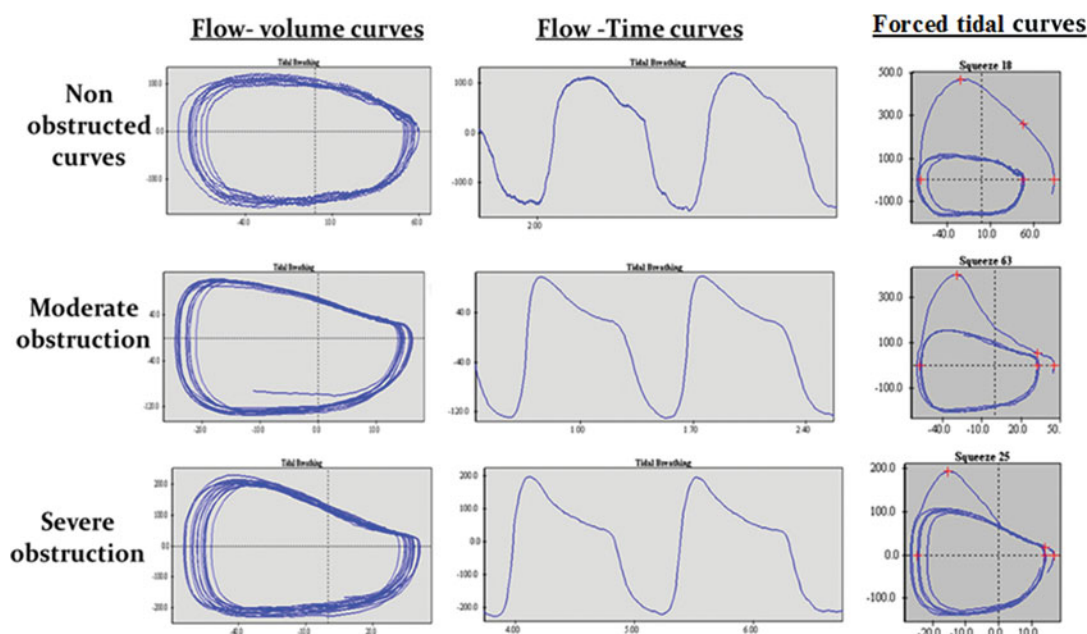


Figure 1. Examples of tidal breathing, flow-volume and flow-time curves and the corresponding forced tidal curves with the associated point known as “ $\dot{V}_{\text{maxFRC}}$ ” (asterisk seen on graph).

Table 2. Comparison of nonobstructed infants ($\dot{V}_{\text{maxFRC}} > -1$ zscore predicted) to the severely obstructed infants ($\dot{V}_{\text{maxFRC}} \leq -2$ zscore).

N	zscore > −1	zscore ≤ −2	P value	95% CI
	69 Mean (SD)	52 Mean (SD)		
Clinical data				
Age (months)	10.1 (3.8)	10.6 (4.7)	0.593	[−1.9,1.1]
Sex (male)	45 (64.3%)	33 (63.5%)	0.925	
Weight (kg)	8.3 (1.5)	9.3 (1.9)	0.003	[−1.6,−0.3]
Height (cm)	70.2 (5.1)	72.4 (6.2)	0.037	[−4.2,−0.1]
Week of birth	39.1 (1.9)	38.8 (2.2)	0.346	[−0.4,1.2]
Tidal breathing parameters				
RR (min ^{−1})	34.6 (10.3)	34.1 (9.7)	0.756	[−3.1,4.2]
t _i /t _E	0.77 (0.17)	0.68 (0.20)	0.01	[0.02,0.16]
t _{PTEF} (sec)	0.25 (0.08)	0.20 (0.09)	0.04	[0.002,0.09]
t _{PTEF} /t _E	0.27 (0.07)	0.19 (0.05)	<0.001	[0.05,0.10]
TEF ₅₀ /PTEF	0.89 (0.04)	0.81 (0.07)	<0.001	[0.06,0.10]
TEF ₂₅ /PTEF	0.67 (0.09)	0.55 (0.11)	<0.001	[0.09,0.16]
PTEF (ml/sec)	116.7 (29.6)	129.6 (29.1)	0.021	[−23.5,−2.2]
PTIF (ml/sec)	143.7 (36.8)	165.4 (30.9)	0.021	[3.4,39.9]

RR, respiratory rate; t_i , inspiratory time; t_E , expiratory time; t_{PTEF} , time to peak tidal expiratory flow; TEF_{50} and TEF_{25} , expiratory flow when 50% and 25% of tidal volume remains in the lungs, respectively; PTEF, peak tidal expiratory flow; PTIF, peak tidal inspiratory flow.

It is interesting to note that the differences in respiratory rates between the two groups were insignificant. Among the studied parameters, t_{PTEF}/t_E , $\text{FEF}_{50}/\text{PTEF}$, and $\text{FEF}_{25}/\text{PTEF}$ showed the largest differences between the severely obstructed and the nonobstructed infants. Correlations between each of these parameters and $\dot{V}_{\text{maxFRC}}$ gave r values of 0.61, 0.67, and 0.65, respectively ($p < 0.0001$) (Figure 3).

In an effort to derive a more practical data set, the entire study population was divided into two groups: group I had no to moderate airway obstructions (z-score $\dot{V}_{\text{maxFRC}} > -2$) and group II had severe airway obstructions (z-score $\dot{V}_{\text{maxFRC}} \leq -2$) (Table 3). Average

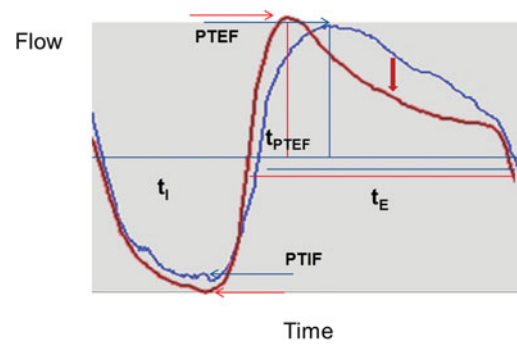


Figure 2. Flow-time tidal breathing curves of obstructed compared to nonobstructed infants. The bolded (red) curve describes airflow in an obstructed infant. An extended expiration time, an earlier time to peak flow and lower expiratory flows in the second part of expiration can be noted in relation to non-bolded (blue) curve which represents the airway flow of an infant with no airway obstruction. There are also higher peak expiratory and inspiratory flows in the curve representations airway obstruction.

t_{PTEF}/t_E , $\text{FEF}_{50}/\text{PTEF}$, and $\text{FEF}_{25}/\text{PTEF}$ values differed significantly ($p < 0.0001$) between groups I and II, similar to the first comparison (nonobstructed versus severely obstructed infants). Box-plot diagrams of these three parameters are shown in Figure 4. ROC curves of these parameters showed AUC values of 0.796, 0.813, and 0.797, respectively (Figure 4). The cutoff values selected for these tests showed high negative predictive values for infants with severe airway obstruction (Table 4): 85.9% for $\text{FEF}_{50}/\text{PTEF}$ and $\text{FEF}_{25}/\text{PTEF}$, and 85.7% for t_{PTEF}/t_E . Because these specific values may be measured slightly differently in other laboratories with different equipment, we also calculated them as z-scores according to the values suitable for our normal testing (z-score $\dot{V}_{\text{maxFRC}} \geq 0.5$). Cutoff value z-scores for $\text{FEF}_{50}/\text{PTEF}$, $\text{FEF}_{25}/\text{PTEF}$, and t_{PTEF}/t_E were calculated as -0.35 , -0.34 , and -0.43 , respectively.

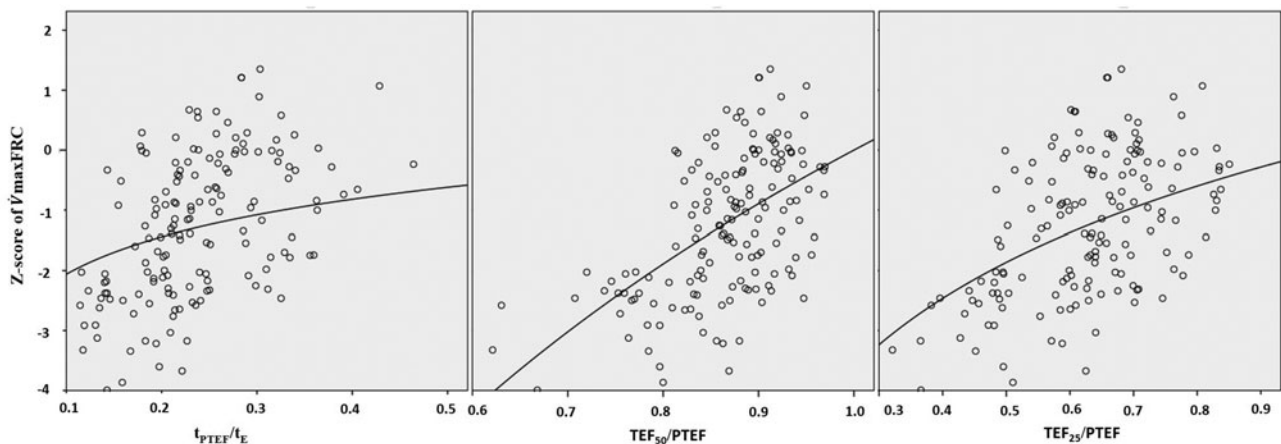


Figure 3. The s-curve correlation between t_{PTEF}/t_E , $\text{TEF}_{50}/\text{PTEF}$ and $\text{TEF}_{25}/\text{PTEF}$ and z-score $\dot{V}_{\text{maxFRC}}$. $R = 0.61, 0.67, 0.65$, respectively, $P < 0.0001$ for all.

Table 3. Comparison of absent to moderately obstructed infants (zscore > -2) to those with severe airway obstruction (zscore ≤ -2).

N	zscore > -2 104 Mean (SD)	zscore ≤ -2 52 Mean (SD)	P value	95% CI
Clinical data				
Age (months)	10.2 (4.2)	10.6 (4.7)	0.675	[-1.8,1.2]
Sex (male)	69 (66.3%)	33 (63.5%)	0.683	
Weight (kg)	8.4 (1.6)	9.3 (1.9)	0.003	[-1.4,-0.3]
Height (cm)	70.4 (5.8)	72.4 (6.2)	0.054	[-3.9,0.0]
Week of birth	39.0 (2.0)	38.8 (2.2)	0.536	[-0.5,1.0]
Tidal breathing parameters				
RR (min⁻¹)	35.0 (10.9)	34.1 (9.7)	0.600	[-2.6,4.5]
t_i/t_E	0.74 (0.18)	0.68 (0.20)	0.04	[0.003,0.117]
t_{PTEF} (sec)	0.26 (0.11)	0.20 (0.09)	0.0122	[0.01,0.11]
t_{PTEF}/t_E	0.26 (0.06)	0.19 (0.05)	<0.001	[0.05,0.09]
TEF₅₀/PTEF	0.89 (0.04)	0.81 (0.07)	<0.001	[0.06,0.09]
TEF₂₅/PTEF	0.67 (0.09)	0.55 (0.11)	<0.001	[0.09,0.15]
PTEF (ml/sec)	117.9 (29.7)	129.6 (29.1)	0.020	[-21.7,-1.8]
PTIF (ml/sec)	146.1 (38.6)	165.4 (30.9)	0.029	[2.1,36.5]

RR, respiratory rate; t_i, inspiratory time; t_E, expiratory time; t_{PTEF}, time to peak tidal expiratory flow; TEF₅₀ and TEF₂₅, expiratory flow when 50% and 25% of tidal volume remains in the lungs, respectively; PTEF, peak tidal expiratory flow; PTIF, peak tidal inspiratory flow.

Discussion

The parameters t_{PTEF}/t_E, FEF₅₀/PTEF, and FEF₂₅/PTEF derived from TB flow and time recordings in infants were positively correlated to $\dot{V}_{maxFRC}$, and could discriminate between infants presenting with severe expiratory airflow obstruction and those without.

The use of TB measurements for evaluating expiratory airway obstruction in infants is compelling. It does not necessitate forced expiration and due to its relative simplicity, may be performed on infants during natural sleep, thus foregoing the need for patient sedation. The test is inexpensive, quick to perform and portable, and it can be performed on infants with severe illnesses who cannot undergo the standard iPFT. Nevertheless, to the best of our knowledge, there has not been any significant clinical use of TB parameter measurements.

TB is a complex phenomenon encompassing not only the mechanical properties of the lungs but also active modulations influenced by peripheral and central breathing control systems (6,7). The measurement of t_{PTEF}/t_E is associated with the initial portion of TB expiration, until the point of peak flow. Morris and Lane (8) were the first to observe that t_{PTEF}/t_E is shortened in obstructed patients. They speculated that this is due to the reduced inhibitory effect of the inspiratory muscles during the initial phase of expiration. Normally, these muscles remain active during this initial phase, reducing chest wall recoil pressure and consequently inhibiting the flow, allowing it to reach its expiratory peak slightly later than without their activation. The physiological explanation for the t_{PTEF} reduction in obstructed patients is most probably to allow additional time for the second part of the expiration, which is more passive, while keeping the total expiration time relatively constant. Indeed, t_{PTEF}/t_E can be reduced in obstructed patients due to shorter

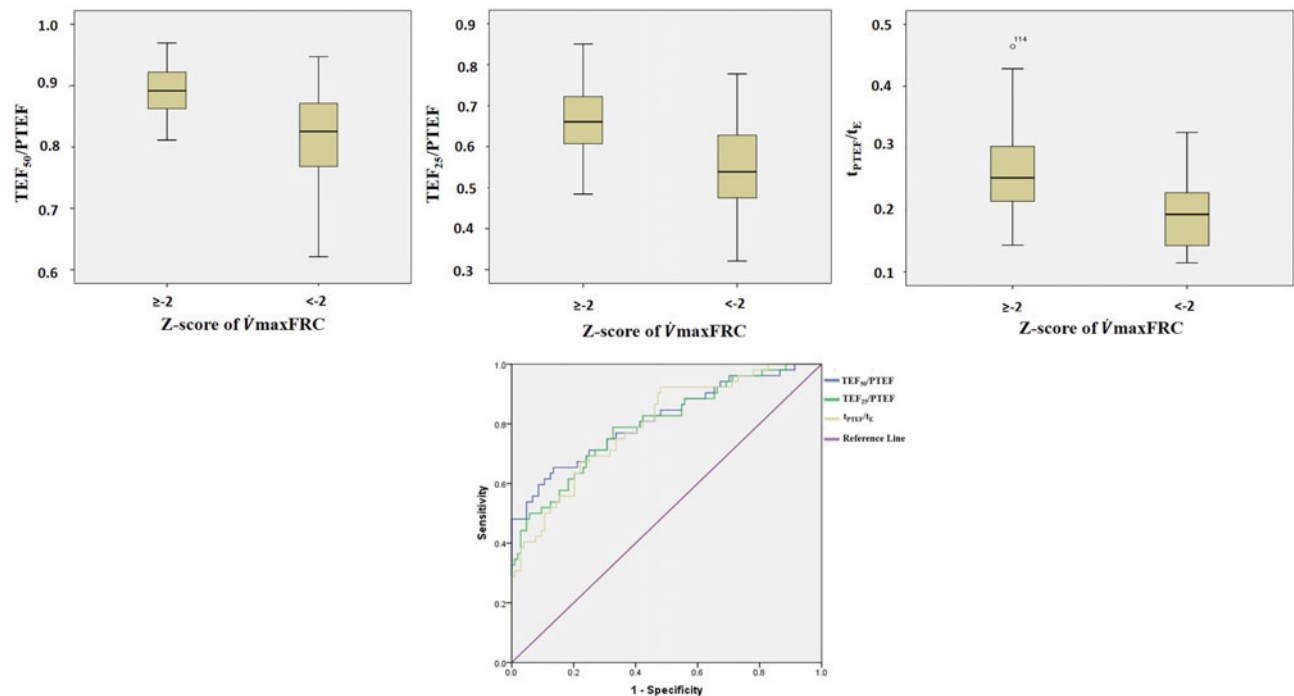


Figure 4. Box-plot diagrams ($TEF_{50}/PTEF$, $TEF_{25}/PTEF$ and t_{PTEF}/t_E with $P < 0.0001$ for all) and receiver operating characteristic curves (ROC) of $TEF_{50}/PTEF$, $TEF_{25}/PTEF$ and t_{PTEF}/t_E for evaluating severe airway obstruction in infants (z-score $\dot{V}_{maxFRC} \leq -2$). The areas under the curve (AUC) are 0.813, 0.797, and 0.796, respectively.

Table 4. The cut-off values of $\text{TEF}_{50}/\text{PTEF}$, $\text{TEF}_{25}/\text{PTEF}$ and $t_{\text{PTEF}}/t_{\text{E}}$, also expressed in Z-score, which were chosen for ruling out severe airway obstruction in infants and their prediction power.

	$\text{TEF}_{50}/\text{PTEF}$	$\text{TEF}_{25}/\text{PTEF}$	$t_{\text{PTEF}}/t_{\text{E}}$
Normal value (SD)	0.896 (0.04)	0.674 (0.09)	0.267 (0.07)
Cut-off value	0.882	0.643	0.237
Cut-off value Z-score	-0.35	-0.34	-0.43
Sensitivity	80.8%	75.0%	69.2%
Specificity	58.7%	60.2%	59.3%
Negative predictive value	85.9%	85.9%	85.7%
Positive predictive value	49.4%	49.4%	48.8%

t_{PTEF} or longer t_{E} , and our data show that both factors are involved. Severely obstructed infants had significantly shorter $t_{\text{I}}/t_{\text{E}}$ ($p = 0.01$) and t_{PTEF} than nonobstructed infants (Table 2). However, when comparing the severely obstructed infants to the group of infants with less severe airway obstructions, the difference in $t_{\text{I}}/t_{\text{E}}$ became less significant ($p = 0.04$), indicating that shorter t_{PTEF} is the dominant effector of the reduced $t_{\text{PTEF}}/t_{\text{E}}$ (Table 3). The value of t_{PTEF} should be interpreted with caution, because it is an absolute number that varies with the infant's age; on the other hand, the proportion $t_{\text{PTEF}}/t_{\text{E}}$ is considered relatively stable after the first 3 months of life (9). A possible mechanism contributing to reduced t_{PTEF} is the release of braking-induced activation of laryngeal adductors, as part of the laryngeal control of expiratory flow. Involvement of chest wall instability in infants and dynamic elevation in FRC has also been suggested (6,10–12).

The reduced flows in the mid to late portion of the expiration ($\text{FEF}_{50}/\text{PTEF}$ and $\text{FEF}_{25}/\text{PTEF}$) are most probably a reflection of the increased expiratory airway resistance in the obstructed patients, as this part is considered more passive.

There is no clear definition in the literature for significant airway obstruction based on $\dot{V}_{\text{maxFRC}}$. In our study, we used z-score $\dot{V}_{\text{maxFRC}} \leq -2$ (from the Hoo Equations (5)) as the classification for severe airway obstruction. Some have used a definition of “tidal breathing limitation” in which the maximal flows generated by forced expiration reach their limit at the tidal flows (lower right picture, Figure 1). However, the number of patients in our study who met this defining criterion was small, and it did not provide better discrimination from the rest of the study group based on TB analysis (data not shown).

The results of our study show a mean (SD) $t_{\text{PTEF}}/t_{\text{E}}$ in nonobstructed infants (z-score $\dot{V}_{\text{maxFRC}} > -1$ predicted) aged 3 to 24 months of 0.27 (0.07). Regarding $\text{FEF}_{25}/\text{PTEF}$ and $\text{FEF}_{50}/\text{PTEF}$, we report mean (SD) values of 0.67 (0.09) and 0.89 (0.04), respectively. Numerous studies have published values for $t_{\text{PTEF}}/t_{\text{E}}$ in healthy infants at different ages ranging from 0.258 to 0.29 (9,13–15). There are far fewer values reported for $\text{FEF}_{25}/\text{PTEF}$ and $\text{FEF}_{50}/\text{PTEF}$. Mean reported values for

healthy term infants are 0.75–0.787 for $\text{FEF}_{25}/\text{PTEF}$ and 0.88–0.920 for $\text{FEF}_{50}/\text{PTEF}$ (16,17). Certain discrepancies, although very minor, exist between our values and those of other groups. We postulate that this is due to the different equipment used for the measurements in the various studies.

The mean respiratory rate (and total time of respiration) remained more or less constant between the significantly obstructed infants and the infants with moderate to no airway obstruction. Our findings concur with those of Morris and Lane (8), who also reported no significant differences in respiratory rate between severely obstructed and healthy adult patients.

Numerous studies have addressed the issue of using TB curves analysis to assess lung function in various diseases. Morris et al. (18) were the first to suggest that certain parameters of TB can be used to indicate airway obstruction. Its use was later demonstrated in asthmatic preschool children where improved $t_{\text{PTEF}}/t_{\text{E}}$ values post-bronchodilator treatment were also shown (10,19). Studies have also suggested that TB flow-volume curves have strong discriminatory power between some lung pathologies (20,21). Multiple groups have shown that $t_{\text{PTEF}}/t_{\text{E}}$ is lower in infants who develop wheezing later in life (22,23). However, other studies have been less successful in using TB analysis to assess lung function. One of those studies, for example, showed that there is no difference in $t_{\text{PTEF}}/t_{\text{E}}$ between healthy neonates and those with cystic fibrosis (24). Our study presents a number of advantages over previous reports. Our study population is larger than in many former publications. In addition, some of these previous studies did not compare TB parameters to direct measurements of airway flow, as compared to forced expiration. Moreover, some of the studies were done in children and adults (7,8,10,14) as opposed to only infants in our study. TB loops may be more informative in infants compared to children and adults because the former's highly compliant respiratory system produces a higher dynamic FRC, thus bringing the TB curves closer to total lung capacity (23).

Our study has several limitations. First, our control group was comprised of infants who were referred for iPFT due to respiratory complaints. Although infants with chronic diseases were excluded, and no expiratory flow obstruction was diagnosed according to $\dot{V}_{\text{maxFRC}}$, these infants cannot be considered completely healthy. Another problem with our study is the use of triclofos sodium which has been shown to slightly increase respiratory rate (25). We must also point out that in the clinical setting, nonsedated infants will not always allow the physician to test them in an ideal manner.

To the best of our knowledge, there has been no significant clinical use made of TB parameter measurements. The method used to obtain these parameters is user-friendly and due to its portability, can be introduced

in settings other than lung function laboratories, such as clinics or emergency rooms.

Conclusion

Our study shows that t_{PTEF}/t_E , $FEF_{50}/PTEF$, and $FEF_{25}/PTEF$ derived from TB curves can provide the clinician with objective information and may serve as a useful tool to rule out severe expiratory airway obstruction in infants.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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