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Review

Clinical Applications of Forced Oscillation Technique (FOT) for Diagnosis and Management of Obstructive Lung Diseases in Children

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Abstract

Obstructive lung diseases such as bronchial asthma, COPD, and cystic fibrosis are a burden on many patients across the globe. Spirometry is considered the gold standard for diagnosing airflow obstruction, but it can be difficult for pediatric patients to do and requires a lot of effort. As a result, healthcare providers need new, effortless methods to diagnose airway obstructions, particularly in young children and individuals unable to perform the spirometry maneuver. The forced oscillation technique is a modern method requiring only tidal breathing combined with the application of external, source of low-amplitude oscillations to evaluate the respiratory system's response. It might be essential for identifying early respiratory changes caused by smoking, childhood asthma, and may prove more sensitive than spirometry in identifying peripheral airway disturbances or evaluating the long-term success of therapy. This review describes the methodology and the indications for the forced oscillation technique and outlines its relevance in clinical practice.

Keywords

airway obstruction, reference values, pulmonary function tests

INTRODUCTION

Obstructive lung diseases are a group of pulmonary disorders that include bronchial asthma, emphysema, chronic bronchitis, bronchiectasis, and cystic fibrosis. These conditions are defined by airflow limitation in the conducting part of the bronchial tree and/or emphysematous changes in the respiratory zone of the lungs.[1] In 2019, the World Health Organization (WHO) identified chronic obstructive pulmonary disease (COPD) as the third greatest cause of death, primarily affecting the elderly population (aged 75 and over).[2] Bronchial asthma, on the other hand, ranks the highest among chronic disorders in children[3,4], particularly preschoolers (5 years old and less). According to research conducted in the United States, the prevalence of emergency visits due to acute wheezing is significantly higher among children aged 0 to 4 than in all other age groups **(Fig. 1)**.

The golden standard of diagnosing obstructive pulmonary conditions is spirometry, but this technique requires specific forced maneuvers and the patient's cooperation. Consequently, it is essential to introduce and validate new diagnostic methods for identifying obstructive lung diseases which are highly informative and at the same time can be easily administered among groups such as preschool children and elderly people. The Forced oscillation technique (FOT) is an advanced method that needs minimal cooperation, and the examination time is considerably reduced. FOT has been effectively used in various pediatric respiratory conditions and could serve as a substitute to spirometry for heterogeneous ventilatory disorders primarily in the small airways.[5-7]

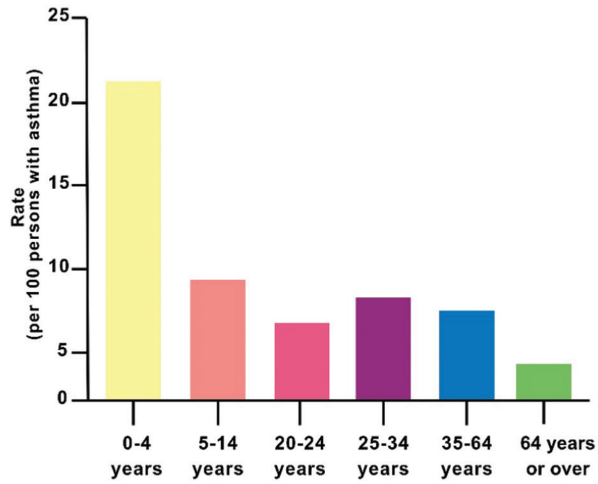

Figure 1. Emergency department visits for acute wheezing (risk-based) in the United States, with data representing age-specific average annual rates for 2007–2008 (U.S. National Surveillance of Asthma report[4]).

History and methodology of FOT

Although different FOT devices have become popular only in the recent years, the methodology of oscillation mechanics of the respiratory system was first introduced in 1956 by DuBois et al., who evaluated the airway response to pressure waves at various frequencies.[8] Forced oscillations are induced by an external force that leads to the vibration of the system (in our case, the respiratory system). The amplitude of the oscillation depends on the frequency of the external force and the system's natural frequency. If the external force's frequency is close to the natural frequency, the amplitude of the oscillation will increase significantly, leading to a phenomenon known as resonance. Nowadays, machines provide portable, simple to use, and effort-independent options that are used by many clinicians. FOT is a non-invasive technique for evaluating respiratory mechanics and airway resistance during tidal breathing. The impedance of the respiratory system is measured by superimposing small-amplitude pressure oscillations on the respiratory system and measuring the resultant oscillatory flow. The pressure waves are derived from a loudspeaker, transported to the patient's airways through a mouthpiece and the nose is obstructed with a nose clip **(Fig. 2)**.

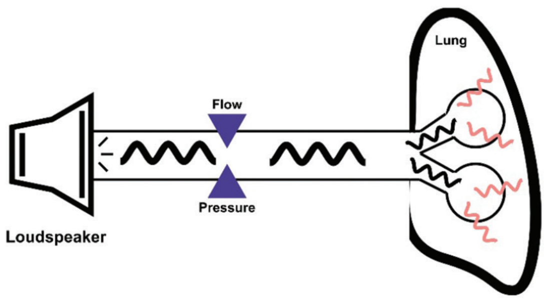

Figure 2. Schematic representation of the structure of a FOT device.[9]

The patient is in a seated position with a neutral or slightly extended position of the head, the hands of the examinator or the patient himself are supporting the cheeks to decrease the oscillations in the upper airways.[10] The test continues for 30 seconds tidal breathing and requires three to five properly executed measurements **(Fig. 3)**.[11,12]

Figure 3. A 7-year-old girl performing FOT using RESMON PRO device.

Main parameters derived from FOT are impedance (Z), resistance (R) and reactance (X). Impedance generalizes the relationship between pressure and airflow. The resistance (R) is the real part of Z that reflects the mechanical properties of the respiratory tree, assessing even the smallest airways. The reactance (X) is imaginary value, which indicates the elastic properties of the respiratory system. At low frequencies, it is negative. The reactance area (AX) is the area between the reactance curve and the abscissa. This is the sum of the reactance at a frequency of 5 Hz to the resonant frequency (Fres) **(Fig. 4)**.

Medium frequencies are used usually for routine clinical application, but the implementation of both low-frequency and high-frequency forced oscillations can help uncover various mechanical properties of the respiratory system, making these techniques promising methods for lung function testing.

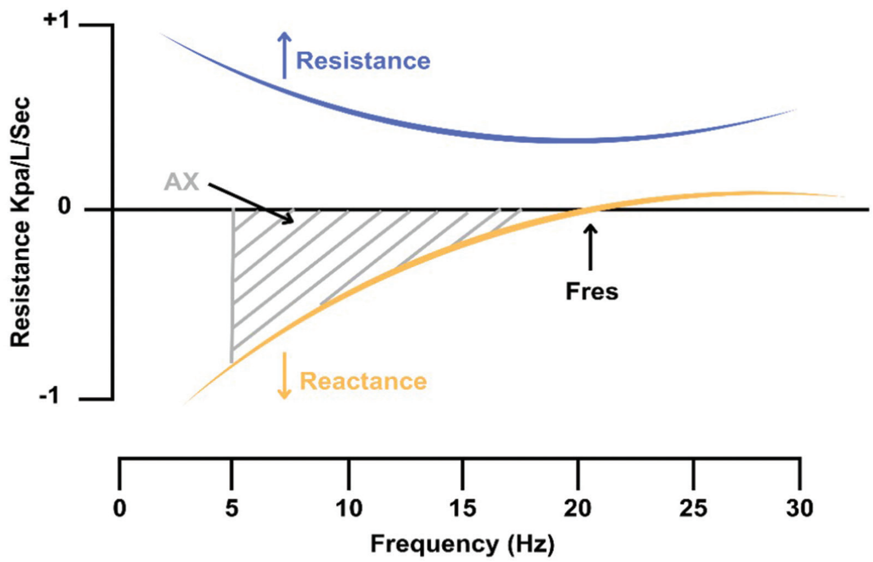

Figure 4. Main parameters of FOT. Blue line: resistance; yellow line: reactance; gray zone: reactance area (AX); Fres: resonant frequency.

Clinical applications of FOT in children

FOT – a most promising alternative to spirometry in bronchial asthma

FOT should be a method of choice for diagnosing asthma, therapy management, and follow-up especially for preschool children, elderly patients, minority groups, and people with neuromuscular diseases who cannot perform spirometry properly. According to Albooshi et al., pulmonologists and pediatricians should change their perspective, understand the role of this new method and learn how to interpret the results. This is the future of better management of childhood asthma.[13] The tidal breathing technique and the brief duration of the test enable experienced physicians to assess children as young as two years old, a feat not achievable with standard spirometry. The success rate for four-year-olds is about 80%, while for healthy children over six years old, it is nearly 100%. The main difficulty is observed in children under 4 years of age even in the presence of a parent. The main problems observed were crying due to fear of the examination and laughter due to the slightly tickling effect of the oscillations in the children's oral cavity. In children with asthma aged three to five years, the success rate ranges from 57% to 100%. When comparing the success rate of FOT to spirometry in kids ages 6 to 8, all of the participants had no trouble with the forced oscillation technique, but only 20% of them were able to do the spirometry maneuvers correctly (own unpublished data).

Several studies have found that young children with stable asthma exhibit impaired baseline lung function when evaluated with FOT, even in the absence of symptoms. Peripheral or proximal obstruction can be detected especially at lower frequencies of 5 Hz, in which the resistance (Rrs) increases. This parameter is also a signal for heterogeneity of pulmonary ventilation. Reactance (Xrs) is not that specific but becomes more negative in distal obstruction and restrictive disorders **(Fig. 5)**.[14]

Additionally, the bronchodilator response measured by FOT can be useful in detecting poor asthma control.[16] Positive bronchodilator response in both children and adults is considered when Rrs5 (resistance of respiratory system at 5 Hz) decreases with 40%, Xrs5 (reactance of respiratory system at 5 Hz) increases with 50% and AX (area of reactance) decreases with 80%.[17]

Reactance parameters proved to be more precise than spirometry in detecting poor asthma control, reinforcing the use of FOT alongside spirometry in clinical asthma management. FOT's feasibility has also been evaluated in bronchoprovocation challenge testing in children, using inhaled adenosine monophosphate (AMP), free running, methacholine, hypertonic saline, cold air, or mannitol challenges. In fact, lower doses of bronchoprovocative agents are needed to trigger significant bronchoconstriction. Schulze et al. demonstrated that resistance increased notably at lower doses of methacholine, even before any changes were detected in FEV_1, indicating that oscillation techniques are more sensitive than spirometry.[18,19]

FOT in the evaluation of patients with cystic fibrosis (CF)

FOT should be considered for evaluation and follow-up of patients with cystic fibrosis. Life expectancy in CF is decreased because the pulmonary engagement worsens over time and the patients have intermittent exacerbations. The pathologic changes are taking place in the small airways with the formation of mucus plugs and plaques, which leads to inflammation, infection, and eventually bronchiectasis. According to the report of Ozturk et al., FOT is more sensitive than spirometry in therapy control and

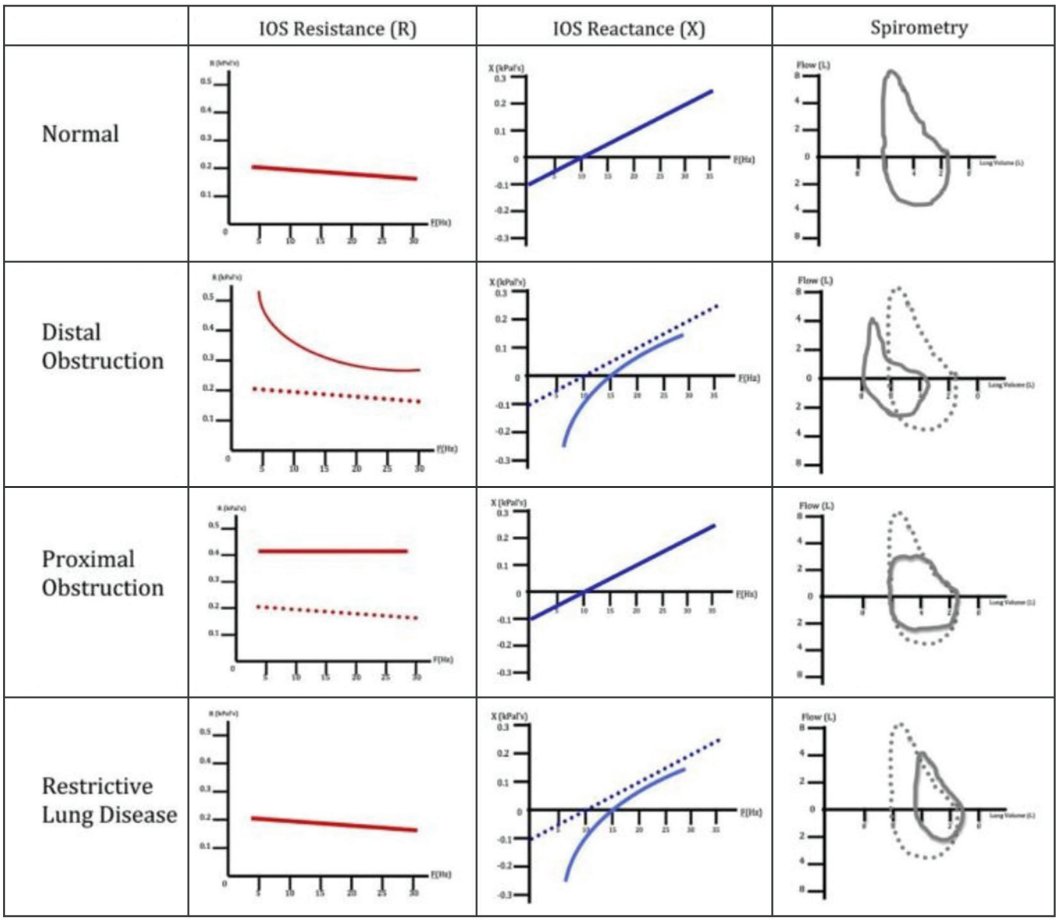

Figure 5. Charts comparing Impulse Oscillometry (IOS) and spirometry in patients with normal, obstructive, and restrictive lung conditions. The dotted lines represent normal tracings, while the solid lines depict pathological tracings[15] (Courtesy of Komarow HD et al., Ann Allergy Asthma Immunol 2011).

there is a significant correlation between symptomatic and asymptomatic patients.[20] Furthermore, their impaired pulmonary status limits their ability to perform the forced maneuvers required for spirometry. There is a significant correlation between FOT and spirometry parameters when evaluating adults on CF transmembrane conductance regulator modulator therapies and the resonant frequency[21] of patient infected with *P. aeruginosa* was higher compared to non-colonized patients. A small study of Lima et al. reports that patients with CF have increased peripheral and total respiratory resistance, increased resistance curve slope, and reduced compliance.[22] However, the role of FOT in the diagnosis of CF is still controversial as many studies suggest that FOT is not better than spirometry in detecting symptomatic patients with CF and fails to detect even severe obstruction.[9,23-25]

Utility of FOT in detection of early lung disease

Some studies report that there is correlation between inflammatory changes in bronchoalveolar lavage (BAL) fluid and FOT parameters.[26] Ramsey et al. discovered that in a study of 184 children monitored over time, an increased BAL neutrophil count was linked to a higher Fres z-score and an increase in Interleukin 8 was correlated with a lower reactance z-score at 8 Hz. However, neutrophil elastase showed no association with any of the FOT measurements.[27]

Numerous studies have assessed various FOT parameters to determine their ability to identify early airway alterations in smokers.[28,29] These studies suggest that the sensitivity of FOT in identifying early airflow obstruction improves when using multiple frequencies. Lower frequencies (5 Hz) are more effective in targeting peripheral airways, while higher frequencies (20 Hz) are confined to proximal airways. Consequently, resistance and reactance at low frequencies (4–6 Hz) are particularly important for identifying smoking-related airway changes compared to higher frequencies. In cases of passive smoking, changes in R5 and R5–20 have been identified as sensitive indicators, especially in adolescents exposed to maternal smoking. Thacher et al. found in their prospective study from 2018 that maternal smoking during pregnancy was linked to the following changes in their children at 16 years of age – lower FEV_1/FVC ratio in spirometry and increased peripheral airway resistance in FOT.[30-32]

The concept of lung function trajectories reveals that early lung diseases in infants and young children may be major risk factors for slower lung development and growth and suboptimal lung function measured in childhood.[33] Decreased spirometry parameters and lower lung functions are predictive of later lung function and of possible risk of clinical diseases like asthma and chronic obstructive pulmonary disease (COPD) in adults.[34] FOT is not a first-choice method in measuring lung function but contributes significantly in understanding the early lung changes in very young and non-cooperative children and this increases the strength of evidence in small airway diseases.

Artificial intelligence (AI) in quality control and interpretation of FOT parameters

The diagnosis of obstructive lung diseases undergoes a severe transformation in the last decade with the development of AI. Using large datasets from diagnostic tests and efficient training algorithms AI can find a pattern, provide interpretation, and differential diagnosis for obstructive diseases. Automated interpretation of the pulmonary function tests (PFT – spirometry, bodyplethysmography and diffusion capacity test), possible with machine learning, gives promising results. The PFT, combined with new methods such as FOT, breath analysis, lung sound analysis, and computed tomography, offers a broader perspective on obstructive diseases.[35]

Several studies have discovered machine learning techniques to detect COPD and assess its severity[36,37], as well as early diagnosis of smoking-induced respiratory changes[38] and bronchial asthma[39]. The possibility of AI to predict asthma exacerbations also is encouraging, leading to decreased clinicians' engagement in reviewing the patient's electronic health record, improved home monitoring and more efficient asthma management.[40] Yu et al. developed AI-based model that was able to accurately detect asthma in children at an early stage, assisting pediatricians in making correct diagnoses. This AI-driven asthma prediction model has significant clinical value and practical importance in improving the diagnosis and appropriate treatment for asthmatic children, while also reducing the misuse of related medications.[41]

AI can be used to detect artifacts caused by coughing, swallowing, and glottis closure with pleasing success. This will decrease the examiner's time needed to exclude breaths and artifacts and will allow the use of FOT in telemedicine and home monitoring.[42]

Specific reference equations for FOT parameters in preschool children

The systematic analysis for the reference equations used in adult Caucasian populations around the world shows a great heterogeneity and for the preschool age there is also insufficient data. The Global Lung Function Initiative (GLI) is collecting FOT data for standardization of the method in order to transform the everyday clinical practice. The creation of reference equations for the different populations requires a proper methodology, a sufficient number of healthy controls and statistical processing. Although there are several articles that try to derive reference equations for healthy Caucasian children under the age of 5, Narchi H and AlBlooshi A[43] focus on the role of collinearity in the statistical approach and note that in these studies, the predicted resistance varied by up to 28%. Many studies report that the main predictive factor for the results in children is height, but other factors such as age, sex, weight, and ethnicity should also be taken into account. The precision and efficiency of the method will improve with the development of appropriate reference equations to set the macro-framework of the normal values of the parameters sought.[15,44-46]

Advantages and disadvantages of FOT

FOT is noninvasive and easy to use. It requires minimal patient cooperation, which is especially beneficial for children and elderly patients.[13] The technique is highly sensitive in detecting early changes in the small airways. This so called "gray zone" is crucial for the early diagnosis and management of respiratory diseases.[47] FOT provides detailed information about both airway resistance and reactance, offering a comprehensive assessment of lung function.[15]

However, some of the lesser disadvantages of FOT are the standardization and the necessity for supplementary testing. There is a lack of standardized protocols for FOT measurements, leading to variability in results across different settings and devices.[43] While the FOT offers valuable insights, it cannot entirely substitute traditional methods like spirometry, which remain essential for comprehensive respiratory assessment.

CONCLUSION

The Forced oscillation technique marks a significant improvement in respiratory diagnostics by offering a non-invasive, sensitive, and comprehensive way to assess lung function especially in preschool age. This diagnostic tool provides a deeper insight into early bronchial changes, leading to prompt diagnosis and therapy. However, due to a lack of applicable reference equations, the collected data are frequently from insufficient numbers of children and do not include those with chronic lung disease follow-up. Therefore, its application among a larger population of both sick and healthy children and adults will increase its predictive value. Spirometry and FOT reflect the characteristics of the individual modalities of bronchial obstruction, and their combination will give us an almost complete picture of the diseases, which is especially valuable in early childhood.

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Клиническое применение метода вынужденных колебаний для диагностики и лечения обструктивных заболеваний лёгких у детей

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Резюме

Обструктивные заболевания лёгких, такие как бронхиальная астма, ХОБЛ и муковисцидоз, являются бременем для многих пациентов по всему миру. Спирометрия считается золотым стандартом для диагностики обструкции дыхательных путей, но это может быть сложно для детей и требует больших усилий. В результате поставщики медицинских услуг нуждаются в новых, простых методах диагностики обструкции дыхательных путей, особенно у маленьких детей и лиц, неспособных выполнить манёвр спирометрии. Метод вынужденных колебаний — это современный метод, требующий только спокойного дыхания в сочетании с применением внешнего источника низкоамплитудных колебаний для оценки реакции дыхательной системы. Он может быть необходим для выявления ранних респираторных изменений, вызванных курением, детской астмой, и может оказаться более чувствительным, чем спирометрия, при выявлении нарушений периферических дыхательных путей или оценке долгосрочного успеха терапии. В этом обзоре описываются методология и показания к применению метода вынужденных колебаний и излагается его значимость в клинической практике.

Ключевые слова

обструкция дыхательных путей, референтные значения, тесты функции лёгких