INVITED COMMENTARY

Can Infant Pulmonary Function Tests be Used as a Screening Tool for Diagnosis of Airway Anomalies in Infants?

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Infant pulmonary function tests (IPFTs) have been performed by specialist centres for more than 40 years. The commonly used IPFTs have been tidal breathing flow volume loops (TBFVL), rapid thoracoabdominal compression (RTC), raised volume RTC (RVRTC), infant plethysmography, multibreath washout and forced oscillation. Although IPFTs have been a great research tool for pediatric pulmonologists, they have limited clinical utility at present. A large international survey showed significant variability in practice on IPFT for clinical purposes and decision making [1]. Centres performing more studies were more likely to do so for clinical purposes.

Some European and North American centres have been using IPFTs (usually RVRTC plus multibreath washout) for clinical monitoring of patients with cystic fibrosis and occasionally for infant interstitial lung diseases. There are sparse data on the utility of IPFTs in phenotyping severe bronchopulmonary dysplasia [2]; follow up of newborns receiving antenatal steroids [3], vascular airway compression [4], and diagnosis or follow up of infants with airway anomalies [5].

In the current issue of *Indian Pediatrics*, Pathania and colleagues [6] publish an exploratory study on IPFTs (Tidal Breathing Flow Volume Loops, TBFVL) in 53 children aged 0-2 years with airway anomalies and compared with controls using Exhalyzer D equipment (Eco Medics, Duernten, Switzerland) and Spiroware-1 software. They correlated TBFVL visual patterns with findings of flexible bronchoscopy. They included infants with isolated laryngomalacia (n = 28), laryngomalacia with additional airway anomalies (n = 24; most of them with associated tracheomalacia, bronchomalacia, or tracheobronchomalacia) and isolated pharyngomalacia (n = 1). Notably, there were no children with other congenital common airway anomalies leading to stridor like vocal cord palsy, isolated subglottic stenosis and vascular airway compression, etc that were included. Infants who were sick or having nasofacial anomalies were excluded due to obvious practical reasons.

The authors describe association between bronchoscopy diagnoses and characteristic TBFVL visual patterns. Isolated laryngomalacia was associated with normal expiratory limb and fluttered inspiratory limb (pattern 3) or a flattened expiratory limb with fluttered inspiratory limb (combined pattern 3 and 4). Those with associated bronchomalacia had a concavity in expiratory loops (pattern 5) and those with associated tracheomalacia had a flattened expiratory limb (pattern 2). There was some overlap amongst various patterns. The authors intended to perform six-month follow-up TBFVL in all subjects, but were only able to present these data in 14 children as their study was interrupted by the COVID pandemic. These limited follow-up data are not presented in detail, but it appears that some children had improvement both in TBFVL visual pattern and clinical assessment. The authors suggest that different graphic patterns in TBFVL may correspond to airway obstruction at a particular site (at the larynx or below the larynx), but are not yet able to identify more specific diagnoses.

The authors are to be congratulated for presenting a relatively large volume of data and attempting to correlate this to bronchoscopy findings of airway obstruction. Their group has a track record for publishing data in this field, including a report of normative data on IPFT in a prospective birth cohort study [7]. However, we feel that as of now TBFVL cannot replace bronchoscopy in the initial investigation of children with suspected upper airway abnormalities.

This study is exploratory with subjective outcomes wherein the authors have classified children according to visual patterns of the TBFVL, but as yet have not provided

standardized criteria for how these visual patterns can be defined and clearly categorized. For the purpose of the study these patterns were characterized by three observers, with discussion and consensus in the case of disagreement, but there is no report of the interobserver variability or any attempt at post-operative validation of these categorizations by a 4th or 5th observer. We know from studies in multiple other fields (e.g. scoring of chest CT abnormalities) that visual pattern recognition often has high variability and poor repeatability [7]. The authors present the results of standard TBFVL parameters, and from this it appears that there are group differences in time to reach peak tidal expiratory flow as a proportion of total expiratory time (tPTEF/tE) between their previously tested controls and children with laryngomalacia and additional lower airway abnormality. However, they have not related this or other objective TBFVL parameters to their visual pattern categorization.

It also appears that there is imperfect concordance between bronchoscopy diagnoses and TBFVL visual patterns emphasizing the need to calculate positive or negative predictive values for the analysis. TBFVL visual patterns also cannot reliably distinguish isolated laryngomalacia from laryngomalacia combined with other lower airway disorders, or tracheomalacia from bronchomalacia.

It must be recognized that IPFT is a highly specialized investigation that requires specific equipment, and a great deal of investigator training and experience. It can only be safely performed in infants with relatively mild symptoms, and is not an option for infants in borderline respiratory failure. These investigations have been available for many decades, but are still only rarely used even in resource rich settings. In contrast, flexible bronchoscopy is widely available, and is a relatively safe procedure provided correct guidelines are followed. A trained bronchoscopist will not have difficulty in correctly identifying and categorizing most of the lower airway abnormalities.

In conclusion, the authors should be congratulated for this novel work which has undoubtedly contributed to the IPFT literature. We hope that they and others are able to take this further with objective classification of different TBFVL visual patterns, assessments of repeatability and interobserver variability, and further investigation of how these correspond to clinical and bronchoscopy findings. We agree with their suggestion that serial IPFT may have future value in assessing whether airway abnormalities are improving. However, at this time we caution against implementing the use of TBFVL visual patterns as a clinical tool.

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