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## Riding a New Wave: Computational Fluid Dynamics Brings Clinical Trials for Tracheomalacia within Reach

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Although tracheomalacia is a widely recognized cause of respiratory morbidity, diagnosis of the condition remains difficult, and prevalence is likely underestimated because of limitations in noninvasive testing (1). Flexible bronchoscopy has long been the gold standard diagnostic test, but because of its invasive nature and because it



requires a careful anesthetic approach (i.e., balancing depth of anesthesia that maximizes patient safety and comfort while allowing spontaneous, unobstructed breathing), it has typically been employed for select patients with moderate to severe symptoms to establish initial diagnosis and less so for subsequent evaluation of disease. Importantly, visual assessment of tracheal collapse via flexible bronchoscopy is subject to significant intra- and interrater variability, even at a qualitative level (2). Confounding these limitations, there is a lack of clarity regarding the “normal” degree of tracheal collapse that is present in healthy infants during inspiration and expiration as well as a lack of data that objectively characterize age-dependent variations.

A noninvasive diagnostic modality that can reliably and quantitatively assess tracheal collapse has long been elusive, with earlier methods, including airway fluoroscopy, contrast tracheobronchography, and computed tomography, falling short in one or more of these parameters. Recently, Hysinger and colleagues validated ultrashort echo time magnetic resonance imaging (UTE MRI) as a means to noninvasively assess tracheomalacia in

neonates without sedation or ionizing radiation, thereby offering an unprecedented opportunity to objectively characterize tracheal dynamics as well as assess changes over time and in response to potential therapies (3). In an editorial accompanying the Hysinger and colleagues manuscript, we noted our optimism with this technology, but we also lamented that UTE MRI “fails to measure the magnitude of force required to produce that collapse,” which is necessary to objectively assess tracheal compliance and determine whether the airway collapse is due to inherent defect in the trachea or excessive forces imposed on it by obstruction in the small airways (4). Though this has yet to be accomplished, an exciting new approach adds a functional component to this structural assessment.

In this issue of *AnnalsATS*, Gunatilaka and colleagues (pp. 1247–1256) demonstrate the utility of UTE MRI to quantify tracheal resistance in infants with tracheomalacia (5). Using computational fluid dynamics (CFD), the authors extracted clinically relevant physiological data from this noninvasive imaging modality, allowing calculation of work of breathing attributed to the defect. This three-dimensional

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DOI: 10.1513/AnnalsATS.202007-847ED

approach facilitates our understanding of respiratory mechanics in general and tracheal mechanics in particular, thus enhancing our current understanding of the pathophysiology underlying tracheomalacia. Traditionally, many clinicians have focused on the importance of expiratory collapse resulting in cough, breath holding spells and impaired airway mucus clearance as the primary components of morbidity in infants with tracheomalacia. Importantly, this study reveals biphasic disadvantages of malacic airways, possibly because of disruptions in airflow and a resultant increase in work of breathing throughout the respiratory cycle.

Though these new findings help to more thoroughly explain the prolonged hospitalizations, ongoing requirements for mechanical ventilation, and higher rates of tracheostomy in neonates with bronchopulmonary dysplasia and tracheomalacia, they also offer the possibility of standardizing clinical management of such patients using objective physiologic data (6). Indeed, the authors demonstrated the efficacy of continuous positive airway pressure support to offload the respiratory muscles and reduce work of breathing by reducing tracheal resistance. If confirmed in a larger cohort, these techniques will have

immediate implications for patient care, potentially providing real-time data to inform decisions about respiratory support in affected neonates. Furthermore, the ability to measure both tracheal resistance and work of breathing attributed to tracheomalacia provides the long-awaited objective and quantifiable outcome measures needed to conduct clinical trials, including those evaluating medical and surgical therapies that have long been utilized but never fully validated (7).

Though the work of Gunatilaka and colleagues demonstrates compelling proof of concept, there are several limitations to be noted. The authors understandably limited their initial study to a small cohort of well-characterized patients, but it will be important to replicate these measures with a larger number of children, encompassing a broader age range and varying severity of disease. For older children, these techniques are likely to require an anesthetic approach similar to that applied during flexible bronchoscopy to obtain reproducible and useful data. As such, the effects of various anesthetic agents on tracheal tone and work of breathing will also have to be characterized. Importantly, cost and availability of resources may be the factors that are most likely to limit

application of these methods in other institutions. Although MRI is a readily available diagnostic tool at most children's hospitals, it is not clear how feasible it would be to replicate these dynamic UTE MRI and modeling techniques outside of the authors' institution, which boasts both unique CFD expertise and a dedicated neonatal MRI scanner. Until commercial protocols are developed and readily available, clinical use will be unattainable for most.

Despite these limitations, the future appears bright for infants and children suffering from tracheomalacia now that quantifiable outcome measures are within reach. Furthermore, UTE MRI and CFD may open doors for other conditions characterized by fixed and dynamic airway obstruction in both the upper and lower airways. The work of Gunatilaka and colleagues may represent the earliest stage of a paradigm shift in airway disease made possible by interconnecting computational analysis, state-of-the-art imaging, and physiologic measures to inform clinical care. Finally, it appears that the time has come to start planning prospective clinical trials for infants and children with tracheomalacia. ■

**Author disclosures** are available with the text of this article at [www.atsjournals.org](http://www.atsjournals.org).

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