

Pulmonary Function Testing in the Coronavirus Disease Era: Lessons and Opportunities

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SEVERE ACUTE RESPIRATORY syndrome coronavirus 2 (SARS-CoV-2), causing coronavirus disease 2019 (COVID-19), is responsible for the ongoing global pandemic infecting over 1 hundred million people worldwide. Since the start of the pandemic, aggressive infection control measures have been instituted in health care facilities and elsewhere to limit the spread of the virus. Considerable effort has been made to determine the modes by which SARS-CoV-2 can be transmitted between people, including whether airborne spread is possible. These concerns led to scrutiny of pulmonary function tests (PFTs) as potential sources of droplet and aerosol generation with severe limitations placed on testing in many places as a result. We discuss lessons learned regarding PFTs in the pandemic era, especially as related to the pediatric population, and how these can be applied for future outbreaks.

At the onset of the pandemic, scant objective data existed on the aerosolization potential of common PFTs, including spirometry. Multiple factors, such as testing equipment, inline filter use, availability of negative pressure rooms, selection of bronchodilator administration method where warranted, and exact procedure being done (exercise challenge versus simple spirometry, e.g.) affect potential risk. Guidance from the American Thoracic Society on safely reopening PFT laboratories has been published with specific guidance on risk mitigation.¹ Although the World Health Organization and Center for Disease Control and Prevention do not categorize PFTs as aerosol generating procedures, other organizations, including the European Respiratory Society, do classify PFTs as such under certain conditions. Certain procedures, such as cardiopulmonary exercise testing and thoracic gas volume measurements by body plethysmography, have been categorized as higher risk procedures.² Most guidelines make no distinction between adult and pediatric patients, outside of those released by the Italian Pediatric Respiratory Society.³ The Society of French Speaking Pulmonologists has issued detailed guidelines on mitigation, procedural techniques, and patients' selection.⁴ As in many other guidelines, the driving force behind performing these tests is the balance between risks and benefits in each individual situation, both to the patient and to the performing respiratory technologist or therapist. Two recent review articles highlight the discordant categoriza-

tions and recommendations between different expert respiratory groups.^{5,6}

Objective data on the transmission risks of common PFTs are starting to become available. The most comprehensive report to date is from the AERATOR study (currently only available on a medical preprint server), where 33 healthy individuals provided cough maneuvers, peak flow, spirometry, and fractional exhaled nitric oxide (FeNO) measurements under well-devised experimental conditions to accurately measure aerosolization.⁷ Cough and unfiltered peak flow measurements produced the highest levels of aerosolization, whereas guideline-adherent spirometry (with a standard filter) and FeNO measurements produced low levels of aerosolization, at equivalent levels to regular peaking. The authors also found that use of cardiopulmonary exercise testing facemask significantly reduced aerosolization due to coughing induced by testing. Hence, the authors conclude that standard PFTs indeed should not be considered aerosol generating procedures and that exercise testing (cardiopulmonary exercise test) facemasks significantly mitigate risks due to procedure-induced coughing.

Disruption of PFT services poses unique challenges in pediatrics. Children are more likely to be asymptomatic during COVID-19 infections, though still capable of viral transmission. This renders symptom-based pretest COVID-19 screening less effective.⁸ Most spirometry in children is done in an office setting, where advanced infection control measures such as negative pressure rooms are unavailable. Operator distancing can also be difficult given the level of coaching and support needed for young children to correctly complete testing. Despite these challenges, many children are poor perceivers of their respiratory symptoms,⁹ which necessitates routine monitoring with objective lung function measurements per established guidelines. Failure to monitor objective measures of lung function may, therefore, place children at elevated risk of loss of asthma control and subsequent exacerbations.

Unique strategies are, therefore, required to obtain needed objective lung function data in pediatric patients. In a clinic setting, PFT operators should be equipped with appropriate personal protective equipment based on their institutional infection control guidelines. COVID-19 testing of all patients beforehand is likely not feasible in an office

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setting but should be considered for higher risk procedures such as exercise stress testing. Nebulization of medications should generally be avoided due to the risk of aerosolization of viral particles. Bronchodilators for testing or treatment purposes should be administered with metered dose inhalers with single use valved holding chambers (and masks as needed). Where the use of nebulizers is unavoidable, filters on tubing and breath-synchronized nebulizers can be used to minimize aerosolization into the environment.¹⁰

Home monitoring could decrease the need for in-clinic testing as well as improve the utility of telehealth for pediatric respiratory patients. Peak flow monitoring has been utilized in the past but may not always identify severe obstruction, rendering it unsuitable to replace spirometry.¹¹ Individual home spirometer units have been distributed to many pediatric and adult cystic fibrosis patients through the CF Foundation during the pandemic. Outside of this indication, however, these units are difficult to obtain due to lack of insurance coverage. Furthermore, children may not be able to provide repeatable and accurate results with these units, though it represents a fertile ground for further research.

Modes of testing that minimize potential aerosolization should be considered. In particular, impulse oscillometry (IOS), a variant of the forced oscillation technique (FOT), is particularly well suited for this purpose. The test requires only normal tidal volume breathing through a filtered pneumotach and, therefore, is less likely to induce coughing and result in aerosolization. IOS measures the mechanical properties of the respiratory system and provides reliable information about both the large and small airways, as well as lung tissue. We have reviewed basic fundamental aspects of this technique and demonstrated its usefulness in clinical practice.¹² Reference ranges are available in children down to preschool ages. More recently, the European Respiratory Society has published updated oscillometry technical standards to address quality control, handling of artifacts, and breathing protocols. Adequate testing requires 3 acceptable repeatable quality measurements, with high reproducibility criteria reflected by low coefficient of variation $\leq 15\%$ “within-session” for children and $\leq 10\%$ for adults.¹³

The potential value of this mode of testing in the age of COVID-19 has recently been published elsewhere,¹⁴ yet continued work is needed to promote wider adaptation of IOS/FOT testing as its use is still largely confined to limited tertiary academic centers in the United States and elsewhere. Other limitations include a lack of straightforward comparisons between IOS/FOT results and prior spirometry results as well as difficulty identifying and monitoring restrictive impairments with IOS/FOT.

Multibreath washout tests to assess the lung clearance index (LCI) also use tidal volume breathing and reflect ventilation inhomogeneity that may be more sensitive for small airways disease than spirometry.¹⁵ This metric has been used in numerous cystic fibrosis clinical trials and is gaining momentum in the clinical realm. Testing times are longer than for spirometry or IOS/FOT and, although the LCI may be abnormal in severe asthma, it may not detect mild-or-moderate disease.¹⁶ Testing can be performed across the whole pediatric age range. Since it is dependent on body size, until at least 6 years of age, the relative and not the absolute changes are usually used to provide clinically meaningful conclusion on ventilation inhomogeneity.¹⁷ Until now, LCI has been mainly used as a research tool, but in expe-

rienced respiratory centers, LCI can be an added benefit to spirometry in certain clinical situations, mainly as an end-point measure for the assessment of beneficial effect of clinical as well as pharmacological interventions.

In conclusion, the COVID-19 pandemic has shined a spotlight on the perhaps previously under-recognized subject of infectious hazards related to PFTs. Although disruptions in services have been unfortunate, there is new opportunity to use the data and resources borne of the pandemic to optimize care moving forward. Patients, especially those in pediatrics, can benefit from new innovation and adaptation to expand PFT monitoring in a safe and accurate manner. There remains a crucial need for further ongoing research in these areas.

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