Can we finally use spirometry in the clinical management of infants with respiratory conditions?

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The goal of health professionals working in respiratory medicine is to diagnose and then manage the health of individuals with respiratory conditions. This requires the engagement of a diverse range of professional disciplines, each with their own tool kit that they bring to the table. For Clinical Respiratory Scientists this tool kit revolves around the quantification of the many facets of cardiopulmonary function. We are all familiar with the use of spirometry, its measurement, reporting and interpretation, and it is often the first tool that comes to hand. Yet increasingly it is being recognised that spirometry may not be the best tool for the job[1] and there is a growing awareness that a more thoughtful approach is required.[2]

One of the most challenging areas of clinical respiratory medicine is the management of infants with respiratory conditions. The clinical picture is often obscured by non-specific signs and symptoms, limited direct clinical trials in this clinical population and the highly complex approach needed to obtain objective measures of respiratory function during infancy. While the measurement of infant lung function (ILF) has a long tradition, its use has until recently been limited to highly specialised research centres often using research hardware and software and localised measurement protocols. These limitations have included a lack of availability of commercial equipment and measurement protocols, appropriate reference ranges against which individual patients can be tracked and a lack of evidence on what the minimal clinically important difference is for each ILF test. The first description of the infant version of spirometry (the raised volume rapid thoracic compression technique (RVRTC) was in 1995,[3] and guidelines from the American Thoracic Society (ATS) and European Respiratory Society (ERS) for the measurement of RVRTC were published in 2000 and further refined in 2005.[4 5]

A DECADE ON WHAT HAVE WE ACHIEVED?

A survey of clinical ILF practices carried out in 2010 found that 77% of the 148 respondents worldwide performed RVRTC in a clinical setting.[6] In this survey, a quarter of respondents acknowledged the lack of appropriate reference values as a limitation for performing testing. The lack of guidelines for data interpretation and uncertainty about clinically meaningful changes in the data that would impact patient care and outcomes were also noted as barriers to the effective use of ILF testing in the clinical setting. These barriers were also discussed in a recent ATS/ERS Workshop report,[7] which highlighted that adequate population-based reference data for the RVRTC technique were not available.

The study by Lum *et al*[8] in this edition makes a major step forward in minimising the barriers to using the RVRTC technique in individual patients. This multinational collaboration collated prospectively, collected RVRTC data from healthy infants on the only commercially available RVRTC system, the Jaeger Masterscreen BabyBody by CareFusion. Critically, the authors also investigated the clinical implications of the newly developed RVRTC reference equations for assessing lung function outcomes in infants with cystic fibrosis compared with the historically used reference equations derived from earlier RVRTC equipment.[8 9]

In this study, the authors collated RVRTC data collected using the Jaeger system from London, UK, Newcastle, Australia, Barcelona-Donostia, Spain, and Lisbon, Portugal. The study also examined differences in outcomes from the contemporary Jaeger system with the London in-house research prototype and demonstrated that these outcomes were not comparable. These differences were further highlighted by demonstrating that the Jones *et al*[9] reference values were inappropriate for Jaeger measurements. The authors examined the potential clinical impact of using the new Jaeger reference equations compared with those of Jones *et al* in a group of infants with cystic fibrosis. For this comparison, the Jones *et al* equations appeared to overestimate lung function abnormalities, thus confirming that equipment-specific reference equations are required for accurate data interpretation.

The major implication of this study is the provision of RVRTC reference equations, derived from a large group of healthy, predominantly Caucasian infants (n=198) collected across multiple sites, for the contemporary, commercially available Jaeger Masterscreen BabyBody RVRTC system. The Jaeger system is now the only commercially available RVRTC system and these findings are vital for our ability to move towards using the RVRTC in clinical situations as well as for research studies. Lum *et al*[8] demonstrated that the most commonly used RVRTC equations to date, that of Jones *et al*, are not suitable for the Jaeger system and this was backed by data to demonstrate that the choice of reference equations alone would impact on the interpretation of lung function outcomes of infants with cystic fibrosis. Considered together, these findings provide a very clear direction to those responsible for ILF laboratories; if the laboratory is using Jaeger equipment, the RVRTC reference equation of choice will be those developed by Lum *et al*. The advantage of having equipment-specific equations would mean that all centres using Jaeger equipment will now have reliable published reference data which should reduce concerns regarding lack of normative data.

As the authors have acknowledged, the majority of data is from the London centre (making up more than 50%), and personnel from the other centres included in this study were trained by the London centre, potentially introducing bias to testing procedure. Equally, the infants included in the dataset were predominantly of Caucasian ethnic background and the potential impact of these equations in infants of different ethnic backgrounds is not clear. While the Jaeger-specific reference equations would be more suitable

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for data interpretation when compared with the Jones equation, ILF laboratories should also consider centre differences and continue to recruit healthy infants, particularly those of non-Caucasian backgrounds, where possible, in order to generate multi-ethnic reference equations for RVRTC outcomes. Any data further collected may be used to validate the reference equations presented in this paper.

Can we use infant spirometry clinically? The jury may still be out and more data are needed to help respiratory health professionals reach the point at which we can truly say that spirometry outcomes in infants have real clinical utility in assisting in the management of individual patients. However, these data and the reference equations derived from them take us in the right direction and may be the step needed to shift momentum towards accurate and objective characterisation of forced expiratory flows and volumes in some of our most vulnerable patients.

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