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FRI: in the transition from research to clinical practice

Quantitative imaging of the airways, for example with functional respiratory imaging (FRI), is evolving from a research tool towards a more clinical application. Maarten van den Berge, thoracic physician, talks about his own experiences with this new technique and its potential role in different airway diseases.

Clinical research evaluating inhalation medication has traditionally been performed using spirometry, with FEV1 commonly being used as a primary end point. FEV1 is still considered the gold standard for the functional assessment of airway diseases, both in pharmacological research and in clinical settings.

However, spirometric values are influenced by many confounding factors, such as the patient's effort, the muscle force, and the deep inspiration and forced expiration. In addition, FEV1 measures not only the characteristics of the lower airways, but also those of the upper airway. It fails to detect minor changes induced by anti-inflammatory or bronchodilating agents. Imaging methods like FRI can be used to supplement lung function data.

FRI VERSUS SPIROMETRY

Although many clinical studies indicate changes in respiratory parameters after the administration of the investigated drug, the clinical significance of these changes is not clear. In addition, the measured parameters are occasionally below the lower limit of reported clinical significance.[1] "Spirometry is a much less sensitive technique compared with imaging," Van den Berge added. "In addition, spirometry is a forced maneuver. For example, if the airways collapse during inhalation, the expiratory flow becomes low, and with that the FEV1 lowers too. So, when a drug is given, on average there is little improvement in FEV1."

MAARTEN VAN DEN BERGE

Maarten van den Berge, MD PhD, is a pulmonologist and associate professor at the University Medical Center Groningen, The Netherlands. He is a clinical and translational researcher focusing on genomic approaches to unravel the mechanisms leading to asthma and COPD development and treatment response. Van den Berge is a member of the ERS and director of the ERS Clinical Research Collaborations (CRC). He has published more than 200 manuscripts in international peer-reviewed journals.

Functional imaging techniques offer the possibility of improved visualization of anatomical structures, such as airways, lobe volumes and blood vessels. Van den Berge expects the findings of these imaging techniques to have a much stronger correlation with symptoms and disease severity, compared with spirometry. "With this quantitative CT technique, we can map patients much more accurately, which is also useful for clinical studies."

APPLICATION IN CLINICAL TRIALS

Virtually all treatments for lung diseases are aimed at changing the lung geometry. Bronchodilators and anti-inflammatory compounds are designed to increase the airway lumen. The resulting improvement in lung geometry can be evaluated using these imaging modalities. With functional imaging, it is possible to compare the anti-inflammatory and/or bronchodilating effects of inhalation medication in the central as well as distal airways.

"FRI is a great tool to measure the effect of anti-inflammatory drugs," Van den Berge summarized, based on a recent study he presented in mid-October 2020.[2] "In this study, we looked at a standard treatment for COPD over four weeks. We used FRI, which is probably a more sensitive tool than spirometry. If we had used spirometry, we would have needed very large patient numbers, hundreds or thousands of people, to measure a treatment effect. With the FRI parameters, we can see that the addition of an inhalation corticosteroid provides actual airway dilation. That effect on FRI measurements was statistically significant. Patients gain more volume in their airways and experience less airway resistance."

POSSIBLE INDICATIONS

The study presented by Van den Berg was in the field of COPD, but the same technique can be applied to asthma or other respiratory diseases, such as cystic fibrosis (CF). Van den Berge expects the greatest application of quantitative imaging to be in asthma and COPD. Due to the high resolution of CT, certain pathologies, such as fibrosis and bronchiectasis, can be distinguished very well. An interesting possibility, according to Van den Berge, is to evaluate the effects of an endobronchial intervention on FRI outcomes. In Groningen, the research on these interventions, involving the insertion of valves and coils, is being performed by Van den Berg's colleague, Dirk-Jan Slebos, in collaboration with others.

PICTURE OF THE WHOLE PATIENT

The CT scan, the basis of FRI, provides information not only about the airways, but also about surrounding tissues and organs. Van den Berge mentioned some examples. "The status of the blood vessels gives an indication of the condition of the heart, and the risk of a heart attack. In addition, with CT we can measure bone density, abdominal and visceral fat mass, and muscle mass. With these types of scanning techniques, we will get a lot of additional information in the future about the condition of the patient." In conclusion, these new imaging techniques may provide valuable information about the individual patient's phenotype.

> FRI is a great tool to measure the effect of anti-inflammatory drugs.

REPLACE SPIROMETRY?

For the past 15 years, FEV1 measurements have been the gold standard and are included in the GOLD guidelines. Nowadays, though, medical professionals view the patient in a broader perspective. Is it plausible that in that respect, quantitative imaging will someday replace spirometry? "The future will show us," Van den Berge answered. "It is not inconceivable that we will stop conducting lung function tests, and perform a CT scan instead to determine lung capacity, residual volume, flow characteristics, and emphysema score. We can also determine other parameters using the same method. There is a lot of information to be gathered with quantitative imaging."

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