Impact of incorporating the evaluation of full inflation recommended in the 2019 spirometry standards on the evaluation of spirometry acceptability

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Background

Evaluation of Full Inflation

The 2019 ATS/ERS spirometry standards update provides an objective means for evaluating forced exhalations began from at or close to full inflation.

At the end of forced exhalation (EOFE), the patient is coached to rapidly inspire to full inflation. The volume inhaled, the forced inspiratory vital capacity (FIVC), must be no more than 5% (or 0.100L, whichever is larger) larger than the forced vital capacity (FVC) for the effort to be considered acceptable. This comparison identifies a submaximal inhalation error (SIE) – forced exhalations that start from a lung volume below full inflation.

The acceptability of spirometry measurements using the 2005 acceptability criteria was compared with the acceptability using the updated 2019 acceptability criteria, including the evaluation of full inflation. We sought to determine the prevalence of SIE in clinical trial spirometry data that was rated as QC Grade A or B by the 2005 acceptability and repeatability criteria.

Methods

We reviewed 646 measurements from 162 patients in the first 4 months of a clinical trial where the 2019 spirometry standards for acceptability, including verification of full inflation were enforced. 58 operators from 39 sites made the measurements.

We also evaluated the acceptability of these measurements using the 2005 standards which do not require verification of full inflation. The two ratings were compared and the prevalence of SIE in measurements that would have been rated QC Grade A or B using the 2005 QC criteria is reported.

Main Findings

- The recommendation to compare the FIVC and FVC allows the identification of spirometry measurements where the largest efforts did not start from full inflation.
- 12.8% of spirometry measurements in a clinical trial that required the use of Phase 4 to verify full inflation showed objective evidence of starting from less than full inflation.
- These measurements were generated by 58.3% of the operators and 43.8% of the sites that contributed measurements.
- When these measurements were evaluated using the ATS/ERS 2005 standards they appeared to be of high quality (acceptable and repeatable).
- In clinical trials, the exclusion of spirometry efforts shown to start from less than full inflation will likely reduce intra-subject variability, reduce implausible treatment effects and permit determination of more accurate treatment effects.

Results

We identified 83 measurements (12.8%) that would have been rated Acceptable and Repeatable by the 2005 standards for acceptability that were rated Unacceptable by the 2019 standards because they were shown to start from a lung volume below full inflation. 28 operators from 21 sites made these measurements. This represents 58.3% of the users and 43.8% of the sites that had contributed data.

The comparison of FIVC to FVC in these measurements showed forced exhalations started from an average of 271 mL (SD 128mL) below full inflation (range 106 to 722 mL), representing an average of 8.9% (SD 3.6%) of the FVC (range 5.1 to 18.4% of FVC).

A common finding was the apparent absence of even a start of an inspiratory plateau within the volume-time tracing of the inspiration preceding the forced expiration. The rapid transition from inspiration to forced expiration suggests the operator was not acting on feedback from the subject when the command to start the forced exhalation was given.

Discussion

All 83 measurements were rated Acceptable, demonstrated repeatability of the two largest efforts and were thus considered QC Grade A or B when evaluated by the 2005 acceptability criteria.

Repeatability of the two largest efforts has long been considered evidence that the forced exhalations started from full inflation. These findings demonstrate that repeatability cannot be used as a surrogate for objective assessment of full inflation as recommended in the 2019 ATS/ERS Update of Spirometry Standards.

More than half of the operators from nearly half of the sites contributed measurements demonstrating SIE, suggesting SIE is common.

Adoption of the evaluation of Phase 4 allows objective evaluation of full inflation. Excluding spirometry efforts that do not start from full inflation will likely reduce the intra-subject variability of spirometry results, reduce implausible treatment effects and permit more accurate determination of treatment effects in clinical trials.

Comparison of current YTD data about intra-subject variability in this study with a past asthma study that used ATS/ERS 2005 guidelines for quality evaluation is encouraging (see below)

Comparison of	2005 Guidelines	2019 Guidelines
Within-visit FEV1 variability - end run-in (mL, % of FEV1)	83 mL , 4.9%	49 mL, 2.4%
Coefficient of Variation on therapy	8.3%	4.6%
Percentage of patients showing >15% coefficient of variation on therapy	20.0%	2.2%