Reviewer's report

Title: Relationship between CT air trapping criteria and lung function in small airway impairment quantification

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Reviewer: marie-pierre REVEL

Reviewer's report:

General comment
This study was designed to validate automated CT quantification of air trapping and to define which CT index better described small airways obstruction. SBNT was used as standard of reference.

As mentioned by the authors, there is yet no standardized valid method for quantifying air trapping on CT and this study is thus helpful by demonstrating E/IMLD ratio is the best index for assessing distal obstruction.

At the beginning of the paper it should be explained the reason why the study population was composed by aging healthy volunteers. This is an interesting choice for a population with subtle distal obstruction.

There are no major methodological problems. Indeed, the authors validated their results with a sophisticated functional test, which is the most appropriate test for small airway obstruction.

Most remarks concern the way results are presented, which can gain in clarity. Some editing problems should also be resolved.

Specific comments

Abstract:
The background section is too long, the results section is too short
Background: Some sentences need editing
A1- “to assess this level of obstruction”: Suggestion: “ to assess obstruction at this level”
A2- “to evaluate automated CT air trapping quantification in assessing small airway obstruction using single breath nitrogen test (SBNT) and subsequently determine which CT criteria was the most accurate to predict small airway obstruction”.
This sentence is not very clear
Suggestion: “To evaluate air trapping automated CT quantification for assessing small airway obstruction and determine which CT criteria better correlate with/predict small airway obstruction on single breath nitrogen test (SBNT)”
A3-Methods: This paragraph should be shortened as follows:
Eighty-nine healthy volunteers aged from 60 to 90 year-old underwent spirometrically-gated inspiratory (I) and expiratory (E) CT and PFTs using SBNT, performed on the same day. Air trapping was estimated using dedicated software measuring on inspiratory and expiratory CT low attenuation area (LAA) lung proportion and mean lung density (MLD). CT indexes were compared to SBNT results using the Spearman correlation coefficient and hierarchical dendrogram analysis. In addition, receiver operating characteristic (ROC) curve analysis was performed to determine the optimal air trapping CT criterion defined as dN2 cut-off = 2.5% N2/l.

The equation here is not very explicit. May be a complementary figure with a detailed legend would help. The authors should also more clearly indicate the cutoff value for obstruction on SBNT.

A4- Results: This section should be expanded.

Expiratory MLD (r= indicate here the correlation coefficient value) and LAA were positively or negatively correlated with SBNT results. Expiratory to inspiratory MLD ratio (E/I MLD) showed the highest AUC value for small airway obstruction assessment.

A5- Conclusion: Should be in one sentence.

All the usual criteria for air trapping quantification were correlated (This should be previously indicated in the result section) with small airways obstruction.

The single sentence could be: Among all CT criteria, all correlating with small airway obstruction on SBNT, E/I MLD was the most suitable criterion for its expression.

Introduction

I 1-Some editing is required
- For instance “to accurately discriminate patients” instead of “to discriminate patients accurately”
- “namely “the lung’s quiet zone”” meaning of the sentence?
- Post- processing instead of post- treatment

I2- Indicate the corresponding references for this “Both a decrease in mean lung density and the percentage of low attenuation area on expiratory CT have been used in various studies and correlated with disease severity in COPD and asthma”

I3- This sentence needs rewriting.” However, the choice of one of these criteria may well affect the way modifications are viewed and there is, therefore, a crucial need for standardization in CT air trapping expression.”

I4- The study purpose needs editing:

This prospective study was designed firstly to explore the validity of air
trapping automated CT quantification for the assessment of small airways obstruction, by using SBNT as standard of reference and, secondly, to assess which was the most accurate CT criterion

Methods
M1-Typo: Lung aging not ageing
M2- Quantitative assessment of air trapping by CT
Editing is required
Indicate whether the air contained within the segmental bronchi were excluded prior to measurement of LAA and MLD.

M3-Statistical analysis Try to simply explain (on a schematic curve?) the meaning of “dN2 cut-off = 2.5% N2/l”
What is N2/l?

Results
R1- Among the 101 subjects: add “eligible” 101 subjects

R2- Inter-observer agreement
The concept of inter observer agreement does not seem appropriate here, as we are dealing with automated measurements. Check with your statistician
Why not simply indicating the intra-class correlation coefficient values? (A reference should be given for ICC calculation in the statistical section, such as Shrout and Fleiss method for instance)

R3- Spatial Heterogeneity
Needs editing and clarification
As shown in Figure 1, E/I MLD ratios obtained at all four levels were statistically different (p=0.02) but all (add four) expiratory (MLD?) values remained significantly associated (correlated?) with dN2 (appendix table 2).

R4- Small airway assessment comparison: I suggest another title: Comparison of CT indexes for small airway obstruction assessment
R5- 43 of (add 89) subjects (48,3%) had dN2 value above the cut-off (add value) (2.5% N2/l).

R6-The following section should be edited
“The Spearman correlation test demonstrated the link between CT air trapping quantification whatever the criteria used (E/I, (E-I)/I and E-I LAA% or MLD) and functional testing of small airway obstruction assessed by dN2 (appendix 1) in our population of 89 healthy
subjects aged 60 and older”
I suggest
“All CT indexes (E/I, (E-I)/I and E-I LAA% or MLD correlated with small airways obstruction, as assessed by dN2”

Discussion
D1-The sentence indicating that automated CT air trapping quantification was achievable for all subjects is somewhat contradictory with a previous sentence in the results section stating that only 89 of the 101 eligible subjects adequately performed PFTs and spirometrically-gated inspiratory and expiratory CT. Please clarify.
D2-Does “inert gas washout tests “ refer to SBNT? if yes, add “such as SBNT”

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
'I declare that I have no competing interests'