Reviewer's report

Title: Prognostic value of alveolar volume in systolic heart failure: a prospective observational study

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Reviewer: Guelmisal Gueder

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In this prospective cohort study the prognostic significance of the lung function variable “alveolar volume” (VA) was analyzed in 260 consecutive patients hospitalized for systolic HF.

The authors found out that reduced levels of VA were associated with a higher comorbidity burden and with increased mortality in univariate and multivariate analysis.

The authors should be lauded for their idea to analyse lung function variables other than spirometric data in patients with heart failure (HF). Although the value of diffusion capacity in HF had been repeatedly explored, alveolar volume was so far not highlighted.

The paper is well written and comprises a variety of different lung function variables. In clinical practice lung function is often restricted to spirometric data only but at present the results are not convincing enough to stimulate readers to invest in further diagnostic procedures as diffusion capacity and bodylethysmography.

I have the following comments:

Major comments:

1. HF is associated with both, restrictive and obstructive ventilatory alterations. VA might indeed represent better than most other variables the combined affection of both ventilatory disorders on pulmonary function.

However currently it is unclear whether VA adds incremental prognostic value on standard lung function parameters as the “forced expiratory volume in 1 sec” (FEV1) or the ratio of “FEV1 and forced (or slow) vital capacity” (FVC, SVC) in patients with HF.

To convince the readers to perform extensive pulmonary function testing in HF the prognostic benefit of VA compared to FEV1 and FEV1/FVC (or FEV1/SVC) should be explored. Furthermore a direct comparison to total lung capacity would be desirable.

2. In the present cohort patients with decreased alveolar volume (VA, <80% of predicted) were older, had more severe heart failure (higher NYHA-class) and more often restrictive and obstructive disorders. “Restrictive disorder” was
defined as a TLC % of predicted below the 5th percentile and a normal ratio between FEV1% and SVC.

Also FEV1% predicted was lower in patients with a VA # 80% predicted.

So it seems that the main effect of VA is rather driven by pulmonary restriction. Please comment.

3. Another concern is that the single breath method used in this study to determine VA necessitates a 10-second breathhold. This reviewer had the experience that HF patients with dyspnea at rest (NYHA IV) were very often not capable to perform the test, which restricts the applicability of the variable. Please comment.

Minor comments:

4. Please explain exactly how confounders were identified for multivariate Cox regression analysis. Which variables were tested univariately? All variables of table 1?

5. In a non-randomized study, adjusted mortality analysis should be depicted instead of Kaplan Meier analysis. Please adapt figure 1 accordingly.

6. Please mention the most important determinants of reduced VA.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.