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COPD

Significant Differences in Body Plethysmography Measurements Between Hospitals in Patients Referred for Bronchoscopic Lung Volume Reduction

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Abstract

During the evaluation of potential bronchoscopic lung volume reduction (BLVR) candidates in our hospital, we frequently observe patients with a lower residual volume (RV) value compared to the value measured in their referring hospital, although both measured by body plethysmography. We explored to what degree RV and other pulmonary function measurements match between referring hospitals and our hospital. We retrospectively analyzed a total of 300 patients with severe emphysema [38% male, median age 62 years (range 38–81), median forced expiratory volume in 1 s 29% (range 14–65) of predicted, and a median of 40 packyears (range 2–125)]. We measured a median RV of 4.47 l (range 1.70–7.57), which was a median 310 ml lower than in the referring hospitals (range −3.04 to +1.94), $P<0.001$). In conclusion, this retrospective analysis demonstrated differences in RV measurements between different hospitals in patients with severe emphysema. Overestimation of RV can lead to unnecessary referrals for BLVR and potential treatment failures. To avoid disappointment and unnecessary hospital visits, it is important that body plethysmography measurements are accurately performed by applying preferably the unlinked method in these patients.

Keywords Body plethysmography · Bronchoscopic lung volume reduction · Emphysema · Residual volume

Introduction

Bronchoscopic lung volume reduction (BLVR) is a valid treatment option for selected patients with severe emphysema [1, 2]. Besides having significant emphysema, the key selection criterion for this treatment is the presence of severe static lung hyperinflation, defined as residual volume (RV) of > 175% of the predicted value [3]. Measuring RV can be performed using body plethysmography, helium gas dilution, nitrogen washout and quantification of lung volumes on a thoracic CT scan, but all can be technically challenging [4]. In patients with severe emphysema, body plethysmography is the preferred method to measure RV, as gas dilution techniques tend to underestimate lung volumes in patients with obstructive lung disease and as CT scan imaging needs full expiration, which is difficult to accurately monitor in the radiology lab [5].

During the evaluation of potential BLVR candidates in our hospital, a BLVR expert center, we frequently observe patients with a lower RV value compared to the value measured in their referring hospital, although both measured by body plethysmography. When the RV value is too low for BLVR treatment, this may lead to disappointment of patients and their caregivers, together with unnecessary, time-consuming and expensive hospital visits, and even wrong treatment selection. We therefore explored to what degree RV and other pulmonary function measurements match between referring hospitals and our hospital, where we strictly adhere to the published guidelines.

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Methods

Using a retrospective analysis, we included patients with severe emphysema who were referred from 62 different hospitals in the Netherlands to our hospital for BLVR evaluation between June 2012 and September 2017. Patients who had both body plethysmography and spirometry measurements available in their referring hospital, as well as in our hospital, within an interval of less than one year between these measurements were included. In our hospital, spirometry and body plethysmography (MasterScreen™, Vyaire Medical, Mettawa, USA) were performed according to the American Thoracic Society (ATS)/European Respiratory Society (ERS) standards [4, 6]. The equipment and guidelines used in the referring hospitals were unknown. Data are presented as median (range). Differences in lung function outcomes between referring hospitals and our hospital were analyzed with a Wilcoxon Signed Rank test. The association between differences in RV and time between measurements in referring hospitals and our hospital was assessed using Spearman's Rho. This analysis was part of a study which was approved by our local medical ethics committee. The study was conducted in accordance with the Declaration of Helsinki.

Results

A total of 300 patients with severe emphysema [38% male, median age 62 years (range 38–81), median forced expiratory volume in 1 s (FEV_1) 29% (range 14–65) of predicted, and a median of 40 packyears (range 2–125)] were included.

We measured a median RV of 4.47 l (range 1.70–7.57), which was a median 310 ml lower than in the referring hospitals (range −3.04 to +1.94), $P<0.001$). Furthermore, we observed significantly higher vital capacity (VC), lower total lung capacity (TLC), and lower intrathoracic gas volume (ITGV) than the referring hospitals (Table 1).

Median time between RV measurements was 118 days (23–364). There was no correlation between differences in RV and time between both measurements (Spearman's rho = 0.06, $P=0.29$).

Of the patients with an RV higher than 175% of predicted in their referring hospital, 34 patients (11%) were not accepted for BLVR treatment due to an RV less than 175% of predicted when re-measured in our hospital. In addition, 133 out of 300 (44%) patients had a larger difference in RV between hospitals than the established minimal important difference (MID) (> 400 ml decrease) [7]. In comparison, 30 out of 300 (10%) patients had a lower RV in the referring hospital, compared to our hospital that was larger than the MID.

A selection of patients ($n=82$) underwent a second body plethysmography measurement in our hospital within one year (often for clinical trial purposes), with a median time between measurements of 69 days (7–352). There was no significant difference between the two RV measurements within our hospital [median difference 0.07 l ($P=0.43$)].

Discussion

Eleven percent of patients who were referred for treatment were directly excluded from BLVR treatment because of lower RV outcomes in our hospital. Our findings are in line with previous research performed in children by Paton et al. who compared spirometry and plethysmography outcomes between different hospitals and also found significant differences in RV and TLC even after standardization of procedures and equipment between hospitals without finding a significant difference in spirometry outcomes [8].

There are several possible explanations for the between hospital differences in RV. Different body plethysmography

Table 1 Pulmonary function outcomes

	N	Referring hospitals	Our hospital	Median difference	P value
RV (l)	300	4.84 (1.75–9.89)	4.47 (1.70–7.57)	0.31 (− 3.04–1.94)	$P<0.001$
RV%pred (%)	299	224 (98–392)	212 (107–350)	15 (− 119–171)	$P<0.001$
TLC (l)	297	7.58 (4.19–12.7)	7.47 (4.21–12.1)	0.11 (− 2.63–4.69)	$P<0.001$
RV/TLC (ratio)	297	0.63 (0.40–0.87)	0.59 (0.34–0.80)	0.04 (− 0.34–0.14)	$P<0.001$
VC (l)	281	2.75 (1.11–6.46)	3.02 (1.46–6.77)	0.20 (− 1.18–3.65)	$P<0.001$
ITGV (l)	257	5.71 (1.74–11.0)	5.63 (2.41–10.2)	0.07 (− 3.11–3.03)	$P=0.01$
FEV_1 (l)	298	0.81 (0.34–2.17)	0.82 (0.35–2.50)	0.01 (− 0.64–1.25)	$P=0.10$
FEV_1%pred (%)	298	29 (14–65)	31 (15–73)	0.87 (− 17–35)	$P<0.01$

Data are presented as median (range). Differences between referring hospitals and our hospital were analyzed with a Wilcoxon Signed Rank test

N number of patients, *RV* residual volume, *%pred* percentage of predicted, *VC* vital capacity, *TLC* total lung capacity, *ITGV* intra thoracic gas volume, *FEV_1* forced expiratory volume in 1 s measurement techniques could have been applied. This is supported by statistically significant differences in both VC as well as ITGV outcomes between our hospital and the referral hospitals. Different approaches could be the use of linked versus unlinked VC maneuvers [9]. Potentially, time between measurements and thus progression of disease could have led to the difference between RV outcomes, but this would result in an increase of RV instead of a decrease. We did not find a significant association between time between measurements and RV. A selection of patients ($n=82$) underwent a second body plethysmography measurement in our hospital just before BLVR treatment. There was no significant difference in absolute RV outcome within an interval of 1 year, suggesting RV measurement consistency in our hospital.

We applied an RV 175% of predicted threshold for BLVR eligibility, which was based on the 2019 BLVR expert panel recommendations and in line with the latest published clinical trial investigating EBV treatment (LIBERATE) [10, 11].

This study has several limitations. First, an arbitrary maximum interval of 1 year between two plethysmography measurements was used; however when using a 6-month interval, absolute RV between hospitals was still significantly different ($P<0.001$, $n=222$). Secondly, we were not aware of patient conditions when they performed the measurement in their referring hospital, which could have influenced RV outcomes. Possibly, body plethysmography measurements in referring hospitals were performed during exacerbations of disease, leading to higher RV outcomes in the referring hospitals [12, 13]. Thirdly, we could not verify that all body plethysmography measurements in the referring hospitals were performed after bronchodilator administration and we were unaware of the guidelines and equipment used. Fourthly, even though the application of the unlinked method probably resulted in lower RV outcomes in our hospital, compared to the referring hospitals, we did not have data available supporting improved patient outcomes after BLVR as a consequence of this technique.

Based on our clinical experience, we have the following suggestions to reduce overestimation of RV in severe emphysema patients during body plethysmography measurement. First, the pulmonary function technician who performs the measurement should take a considerate amount of time to ensure that patients achieve a full expiration state when performing the ERV maneuver during the inspiratory VC measurement. Secondly, the presence of dynamic hyperinflation should be prevented by reducing physical effort just before measurement as well as allowing the patient to get off the mouthpiece between maneuvers [14]. Thirdly, we suggest the use of the unlinked manoeuver. This means that directly after the ITGV manoeuver, the IC measurement will be performed and that the maximum VC measured during spirometry is used for the calculation of RV. Particularly for patients with severe emphysema, it is difficult to perform a maximal VC manoeuver directly after the ITGV manoeuver, resulting in an underestimation of VC and therefore an overestimation of RV. Finally, we suggest that the measurement is performed in a stable state after optimal bronchodilation.

The estimation of lung volumes using quantitative CT analysis could become a valuable tool in the future [15]. However, this method relies heavily on both the quality of the analyzed scans as well as reaching a full inspiration and expiration state during scanning.

Conclusion

In conclusion, this retrospective analysis demonstrated differences in RV measurements between different hospitals in patients with severe emphysema. Overestimation of RV can lead to unnecessary referrals for BLVR and potential treatment failures. To avoid disappointment and unnecessary hospital visits, it is important that body plethysmography measurements are accurately performed by applying preferably the unlinked method in these patients.

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Compliance with Ethical Standards

Conflicts of interest JBAW, JEH, NTH, SWSA, HAMK, and KK declare that they have no competing interests. DJS is a physician advisor and investigator for PulmonX Inc., USA; Nuvaira Inc., USA; CSA Medical, USA; PneumRx/BTG, USA/UK; and FreeFlowMedical, USA, all outside the submitted work.

Ethics Approval This retrospective analysis was part of a study which was approved by our local (University Medical Center Groningen) medical ethics committee. The study was conducted in accordance with the Declaration of Helsinki.

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