# Changes in dynamic lung mechanics after lung volume reduction coil treatment of severe emphysema


## ABSTRACT

We assessed the relationships between changes in lung compliance, lung volumes and dynamic hyperinflation in patients with emphysema who underwent bronchoscopic treatment with nitinol coils (coil treatment) (n=11) or received usual care (UC) (n=11). Compared with UC, coil treatment resulted in decreased dynamic lung compliance ($C_{Ldyn}$) (p=0.03) and increased endurance time (p=0.010). The change in $C_{Ldyn}$ was associated with significant improvement in $FEV_1$ and FVC, with reduction in residual volume and intrinsic positive end-expiratory pressure, and with increased inspiratory capacity at rest/ and at exercise. The increase in end-expiratory lung volume (EELV) during exercise ($EELV_{dyn-ch}=EELV_{isotime}$ $EELV_{rest}$) demonstrated significant attenuation after coil treatment (p=0.02).


## INTRODUCTION

Lung volume reduction by coil treatment in severe emphysema aims to improve lung function, exercise capacity and quality of life.[1 2] Memory-shaped nitinol coils are inserted into subsegmental airways, compressing local emphysematous tissue to increase elastic recoil in adjacent lung areas. Randomised controlled trials (RCT) have shown that coil treatment is superior to usual care (UC) and is associated with sustained improvements in lung function, dyspnoea and quality of life.[3–5] However, the mechanism of action has not been elucidated in a dedicated study assessing the impact of coil treatment on lung mechanics. In this prospective study, we tested the hypothesis that coil treatment induces changes in lung compliance ($C_L$) and analysed the relationships between changes in $C_L$ and in static lung volumes, dynamic hyperinflation and exercise capacity.

## METHODS

Consecutive patients who participated in two successive RCTs comparing bronchoscopic bilateral treatment of emphysema with nitinol wire coils (PneumRx, California, USA) to UC were included in this prospective study. The study was approved by the institutional board of Nice University Hospital (Sud-Mediterranée V-EC-13.051); all patients gave written informed consent. Exploratory tests were conducted at baseline and at 6 months. Pulmonary function testing was conducted with automated instrumentation (Medisoft, Belgium). Balloon mounted catheters were used to measure oesophageal, gastric pressures which allowed the measurement of lung mechanics (ie, quasi-static ($C_{lst}$), dynamic lung compliance during quiet ($C_{Ldyn}$) and at rapid breathing ($C_{Ldyn\ rap}$)). Endurance constant-load cycle ergometry was performed to the limit of tolerance (workload at 70% of the maximal workload reached on previous test). Inspiratory capacity (IC) manoeuvres were performed every minute during ergometry. More details on methods are in the online supplementary file 1.

## STATISTICAL ANALYSIS

Normality of data distribution was assessed by the D'Agostino and Pearson omnibus normality test. Between-groups data were compared using tests for categorical or continuous variables as appropriate. Paired data were evaluated using the paired t-test or the Wilcoxon signed-rank test. The relationships between variables in the coil treatment group were assessed by Pearson's or Spearman's correlation coefficient as appropriate. End-expiratory lung volume (EELV) over time was examined by repeated measures analysis of variance. A $p<0.05$ was considered statistically significant.

## RESULTS

Baseline characteristics of 22 participants (coil treatment (n=11) and UC (n=11)) are shown in online supplementary file 1. Compared with UC, coil treatment resulted in significant improvement in $FEV_1$(L) median (IQR) (+0.055 (−0.015, +0.11) vs −0.030 (−0.065, −0.030), p=0.010) and in residual volume (RV)(L) (1.20 (−1.51, −0.21) vs −0.44 (−0.81, +0.39), p=0.04), RV/total lung capacity (TLC), functional residual capacity (FRC), between baseline and 6 month follow-up (table 1).

$C_{Ldyn}$ significantly decreased after coil treatment compared with UC (table 1, online supplementary file 2). $C_{Ldyn}$ change ($\Delta C_{Ldyn}$) in the coil treatment group correlated significantly with changes in spirometric indices ($FEV_1$, FVC), lung volumes (RV and IC at rest), with $C_{Lst}$ and intrinsic positive end-expiratory pressure (PEEPi), and with IC and IRV at exercise (isotime) (online supplementary file 1 and supplementary file 3). The change (> or ≤ median) in FVC and RV was used to identify responders to coil treatment. Patients who increased FVC and reduced RV (n=5) significantly decreased $C_{Ldyn}$ (%change from baseline) compared with non-responders (−23.0 (−32.5, −20.0) vs 2.65 (−13.0, +1.92), p=0.02). The frequency dependence of lung compliance, $C_{Ldyn\ rap}/C_{Ldyn}$, increased significantly in the coil treatment group, while no significant change was noted in the UC group (table 1).

Peak endurance time (ΔTlim-sec) significantly increased after coil treatment (+28.50 (+20.0, +38.5) vs +2.0 (−15.0, +7.0), p=0.01). ΔTlim in the coil treatment group was significantly associated with changes in $FEV_1$, RV, RV/TLC, FRC, IC-at rest, IRV-at isotime and PEEPi (online supplementary file 1). The increase in EELV during exercise ($EELV_{dyn-ch}=EELV_{isotime}-EELV_{rest}$), a marker of dynamic hyperinflation, demonstrated significant attenuation after coil treatment (p=0.02) (figure 1 and online supplementary file 1).

## DISCUSSION

The mechanism of action of coil treatment has not been fully understood or investigated thus far. Coils are designed to 'roll up' emphysematous lung tissue within target lobes, potentially decreasing regional volume of the hyperinflated lung. An important physiological effect of coils could be elastic lung recoil increase that could, in turn, reduce the time constant for emptying of the respiratory system and thus reduce lung hyperinflation. Our results support this hypothesis. Coil treatment improved dynamic lung mechanics as indicated by reduction in $C_{Ldyn}$ and reduced static lung volumes (RV, FRC and RV/TLC). $C_{Ldyn}$ reduction correlated significantly with changes in expiratory flow ($FEV_1$, FVC) and with indices of dynamic hyperinflation (IC and IRV-at isotime).

The post-treatment reduction in RV correlated with $\Delta C_{Ldyn}$ and was greater than TLC reduction, thus reducing the RV/TLC ratio. We posit that expiratory muscle strength would not increase from treatment, thus RV reduction should be attributed to post-coil treatment shifts in lung compliance, resulting in decreased airway collapse and increased expiratory airflow during active expiration.

We believe this can further be explained by a larger treatment-driven improvement in dynamic versus static lung mechanics, since expiratory flow restriction is a critical determinant of RV in emphysematous lungs. In fact, $\Delta C_{Ldyn}$ in coil-treated patients was significantly correlated with changes in RV, $FEV_1$, FVC and IC at rest, whereas $\Delta C_{Lst}$ was not associated with any

**Table 1** Change (Δ) in lung mechanics parameters from baseline to 6 months follow-up

| | Coil treatment (n=10)* | Usual care (n=11) | p Value |
|---|---|---|---|
| Pulmonary function | | | |
| Δ$FEV_1$, %pred | +2.0 (−0.5, +4.0) | −1.0 (−2.0, −1.0) | 0.01 |
| ΔFVC, %pred | +9.5 (−0.20, +18.5) | +5.0 (−6.5, +9.3) | 0.31 |
| Δ$FEV_1$/FVC, %pred | −1.0 (−4.3, −0.25) | −3.5 (−4.7, −1.0) | 0.20 |
| ΔRV, %pred | −49.5 (−62.9, −6.9) | −19.0 (−35.0, +17.2) | 0.048 |
| ΔTLC, %pred | −5.5 (−15.5, −0.3) | −4.0 (−8.2, +0.5) | 0.26 |
| ΔRV/TLC, %pred | −13.5 (−34.5, −6.7) | −3.8 (−9.7, +7.6) | 0.043 |
| ΔFRC, %pred | −27.0 (−40.5, −16.0) | −6.0 (−15.5, +20.2) | 0.03 |
| Lung mechanics | | | |
| Δ$C_{Lst}$, L/cm$H_2O$ [%] | −13.1 (−25.9, +4.80) | +0.2 (−21.1, +16.0) | 0.21 |
| Δ$C_{Ldyn}$, L/cm$H_2O$ (%) | −20.0 (−24.3, −6.9) | −1.3 (−3.7, +1.1) | 0.01 |
| Δ$C_{Ldyn\ rap}$/$C_{Ldyn}$, % | +6.5 (+3.7, +11.7) | +1.8 (−1.6, +10.4) | 0.043 |
| Δ$Res_{pulm}$, cm$H_2O$/L/s (%) | −6.0 (−11.8, −3.0) | −0.9 (−2.5, +8.8) | 0.57 |
| ΔPEEPi, cm$H_2O$ (%) | −10.5 (−17.3, −6.5) | −4.8 (−6.7, +13.2) | 0.09 |
| Respiratory muscle strength | | | |
| ΔSniff Pes, cm$H_2O$ (%) | +27.8 (+19.5, +43.5) | −0.2 (−8.0, +14.7) | 0.01 |
| ΔSniff Pdi, cm$H_2O$ (%) | +12.0 (−1.4, +15.3) | −1.0 (−8.6, +10.4) | 0.052 |

The (%) indicates the percentage change from baseline at follow-up.
*One patient died from acute mesenteric ischaemia 1 month after coil treatment; one patient in each group has not performed test of lung mechanics at follow-up.
Values represent median (25%, 75% IQR).
p Value for the difference between the groups.
$C_{Lst}$, static lung compliance; $C_{Ldyn}$, dynamic lung compliance; $C_{Ldyn\ rap}$, dynamic lung compliance during rapid breathing; $C_{Ldyn\ rap}$/$C_{Ldyn}$, expresses the frequency dependence of lung compliance; FRC, functional residual capacity; Pdi, transdiaphragmatic pressure; PEEPi, intrinsic positive end-expiratory pressure; Pes, oesophageal pressure; $Res_{pulm}$, pulmonary flow resistance; RV, residual volume; TLC, total lung capacity.

variable.

Furthermore, $C_{Ldynrap}/C_{Ldyn}$ which expresses the frequency dependence of dynamic lung compliance and is considered to represent a measure of resistance to airflow in the small airways[6] increased post-coil treatment; we assume that small airways were likely less prone to dynamic collapse after coil treatment. Notably, in a previous study, Kloosters *et al* reported decrease in volume dependent-airway resistance during dynamic conditions following coil treatment.[7]

In this investigation, the extent of Tlim improvement post-coil treatment was associated with indices indicating decreased static and dynamic hyperinflation (online supplementary file 1). However, the mean Tlim increase of 29.5 s was rather small (ie, 60 s might represent a clinically significant benefit) compared

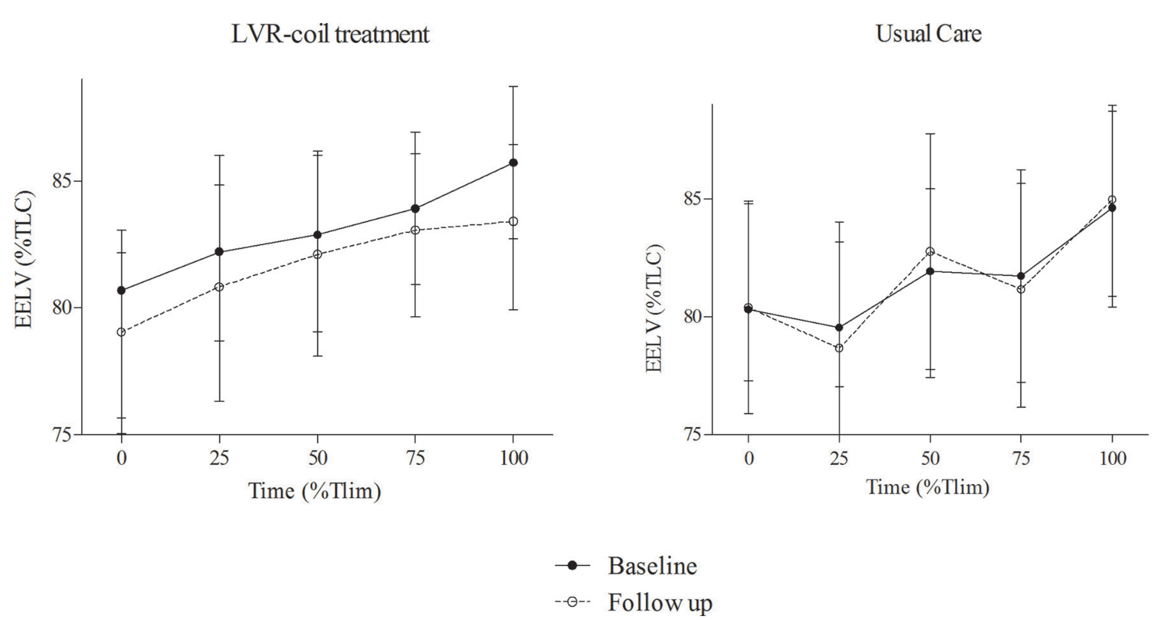


**Figure 1** End-expiratory lung volume (EELV, expressed as % of total lung capacity (TLC)) over time (expressed as % of constant-load cycle endurance time (Tlim); 100% Tlim is isotime) at baseline and at follow-up in coil treatment and usual care group. Data represent mean (SEM) values.

with physiological improvements in lung function or other studies with endobronchial valve placement.[8] This finding is not surprising, because exercise performance is affected by several non-respiratory organ systems (eg, musculoskeletal) and interventions to improve lung function may be of little effect on exercise capacity, where exercise tolerance is limited by leg muscle fatigue.[9 10]

Certain points should be taken into consideration when interpreting our results. Our data provide insight into the physiological changes induced by coil therapy and may provide hypothesis for future studies. The relatively small sample size may have obscured significant clinical or physiological changes between groups in some variables (ie, $C_{Lstat}$) that a larger population might uncover and inequalities between groups (ie, age) may have influenced outcomes. In addition, technical limitations on assessment of $C_{Lstat}$ (mainly assumptions of zero flow during assessment and impact of changes in operating volumes and/or intrinsic PEEP) may explain the absence of significant changes in $C_{Lstat}$ in this study. The use of shutter techniques may have addressed these challenges; in fact, we used both techniques for $C_{Lstat}$ assessment in a preliminary stage but due to poor patient tolerance as has been previously described,[8 10] we finally used a quasi-static method.

In conclusion, our findings suggest that coil treatment reduces static lung volumes and dynamic lung hyperinflation by decreasing lung compliance and dynamic airway collapse in patients with severe emphysema.

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**Contributors** DM had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: DM, SL, HG, GD and CHM. Acquisition of data: DM, SL, JP, JB and CHM. Analysis and interpretation of data: DM, SZ and EZ. Drafting of the manuscript: DM and CHM. Critical revision of the manuscript for important intellectual content: DM, SL, JB, JMP, GD and CHM. Statistical analysis: DM. Study supervision: CHM.

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