



The effect of expiratory flow limitation on supine persistent hyperinflation in COPD: a prospective observational study

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COPD patients demonstrate hyperinflation with failure to increase supine IC and reduced supine IC/TLC ratio compared with healthy controls. Supine persistent hyperinflation strongly correlates with increased expiratory flow limitation. <https://bit.ly/45fh3nX>

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Abstract

Introduction COPD is characterised by airflow obstruction, expiratory airway collapse and closure causing expiratory flow limitation (EFL) and hyperinflation. Supine posture may worsen ventilatory function in COPD, which may cause hyperinflation to persist and contribute to symptoms of orthopnoea and sleep disturbance. Our aim was to determine the impact of supine posture on hyperinflation, dynamic elastance and EFL in COPD and healthy subjects. We hypothesised that changes in hyperinflation in supine posture are influenced by EFL and gas trapping in COPD.

Methods Clinically stable COPD patients (compatible symptoms, smoking >10 pack-years, obstructed spirometry) and healthy controls underwent oscillometry in the seated and supine positions. Hyperinflation was measured by inspiratory capacity (IC) and the ratio of IC to total lung capacity (IC/TLC) while seated and supine EFL was measured as the difference in mean inspiratory and mean expiratory oscillatory reactance at 5 Hz (X_{rs5}). Relationships between IC, IC/TLC and X_{rs5} , were examined by Spearman correlation.

Results 42 COPD patients demonstrated no change in IC/TLC from seated (0.31 L) to supine (0.32 L) position ($p=0.079$) compared to significant increases seen in 14 control subjects (0.37 L seated *versus* 0.44 L supine; $p<0.001$). In COPD, worse dynamic elastance (X_{rs5} r_s 0.499; $p=0.001$) and EFL (ΔX_{rs5} r_s -0.413; $p=0.007$), along with increased age and lower body-mass-index were predictors of supine hyperinflation.

Conclusion Supine persistent hyperinflation occurs in COPD and is associated with increased dynamic elastance and EFL, likely the result of increased airway closure due to gravitational redistribution of lung mass.

Introduction

COPD is a leading cause of morbidity and mortality worldwide. It is characterised by airflow obstruction and expiratory airway collapse and closure which may lead to expiratory flow limitation (EFL), hyperinflation [1, 2] and worse dyspnoea [3–5]. Worsening dyspnoea when lying down is common in COPD but under-recognised and may contribute to overall symptom burden and sleep disturbance, which is also commonly reported in COPD [6–9]. Supine posture causes changes in respiratory mechanics, which likely contribute to worse symptoms and sleep disturbance [10, 11]. Therefore, it would be useful to better understand the mechanical changes that occur in supine posture in COPD, which may be useful treatment targets in the future.



In healthy individuals, inspiratory capacity (IC) increases in the supine position associated with a decrease in functional residual capacity (FRC) [11, 12]. In COPD, there is a failure to decrease FRC, *i.e.* relative supine hyperinflation is present which would result in a failure to increase IC, indicating worse ventilatory impairment and greater work of breathing [11]. Respiratory mechanics are strongly determined by gravity, such that ventilation is increased in dependent lung zones and decreased in areas of airway closure, which is in turn dependent on gravity, ageing and disease. In the supine posture, ventilation and airway closure remain gravity-dependent but are additionally influenced by the decreased FRC, which itself may decrease ventilation through increased airway closure. In COPD, there are additional factors operating which may influence ventilatory function when supine. EFL worsens in the supine position in COPD and supine EFL is associated with more severe airflow obstruction, orthopnoea and nocturnal symptoms [6, 10, 13]. EFL is likely a strong driver of supine hyperinflation, with some COPD patients maintaining an elevated FRC to prevent EFL and to limit airway closure worsening. This could perhaps minimise the work of breathing needed to maintain ventilation.

Respiratory oscillometry is an effort-independent lung function test which involves superimposition of multi-frequency pressure waves over tidal breathing. Respiratory system impedance is measured which comprises two components: resistance (R_{rs}), reflecting overall airway calibre and reactance (X_{rs}), reflecting the elastic properties of the respiratory system under oscillatory (dynamic) conditions. Both R_{rs} and X_{rs} are sensitive to the uneven (heterogeneous) distribution of ventilation in COPD [14]. In addition, both, but particularly X_{rs} , are sensitive to severe airway narrowing, expiratory collapse and airway closure [15–17]. X_{rs} is particularly sensitive because of the reduction in the volume of lung that is accessible to oscillations, making the lungs appear mechanically stiffer under oscillatory conditions (including breathing) *i.e.* higher dynamic elastance, which reflects the increased work of breathing in COPD [15]. Therefore, more negative X_{rs} during tidal volume breathing indicates higher dynamic elastance, which reflects the functional consequences of heterogeneous airway narrowing, airway closure and EFL.

Expiratory airway collapse (and hence EFL) can be measured by looking at expiratory and inspiratory X_{rs} separately. A greater reduction in X_{rs} during expiration reflects increased airway closure and dynamic elastance, giving a greater differential between inspiratory and expiratory X_{rs} (ΔX_{rs}) which accurately predicts EFL. Thus, respiratory oscillometry can provide a highly sensitive measure of EFL during tidal breathing in COPD [16, 18].

The effects of postural change on the interactions between hyperinflation, dynamic elastance and EFL in COPD have not been previously reported. Our aims were therefore, to compare the impacts of supine posture on hyperinflation, dynamic elastance (X_{rs}) and EFL, between COPD and healthy subjects. We also determined potential predictors of supine persistent hyperinflation in COPD and of supine FRC in healthy subjects. We hypothesised that increased dynamic elastance and EFL are associated with supine FRC in COPD, but not in healthy subjects.

Methods

Study subjects

Current or ex-smokers, aged over 40 years with a physician diagnosis of COPD, were recruited from outpatient services at the Royal North Shore Hospital, a large tertiary referral hospital in metropolitan Sydney, Australia, and the Woolcock Institute of Medical Research patient volunteer database. Patients with a recent (<8 weeks) exacerbation of COPD or significant comorbid cardiorespiratory disease were excluded. Diagnosis of COPD was confirmed by a post-bronchodilator forced expiratory volume in 1 s (FEV_1) to forced vital capacity (FVC) ratio ≤ 0.7 or the lower limit of normal, whichever was lower. Healthy subjects were lifelong non-smokers with no symptoms or diagnosis of respiratory disease, no use of respiratory medications and normal spirometry. Ethics approval was obtained prior to patient recruitment from the Northern Sydney Local Health District Human Research Ethics Committee (2021)/ETH01142 and The Bellberry Human Research Ethics Committee (2015-08-603). All subjects provided written informed consent.

Study design

This was a prospective observational study where subjects underwent seated and supine oscillometry measurements. Spirometry and lung volumes were measured following the completion of oscillometry testing.

Physiological measurements

Spirometry and body plethysmography were performed according to American Thoracic Society/European Respiratory Society criteria [19].

Impedance was measured using a TremoFlo oscillometry device (Thorasys Thoracic Medical Systems, Montreal, Canada) as per European Respiratory Society recommendations, using a 5-, 11- and 19-Hz multi-frequency pressure oscillation [20]. Calibration was checked daily using a test load of known resistance and reactance, supplied by the manufacturer. A minimum of three technically acceptable 30-s trials were performed in seated and supine position. Subjects were instructed to breathe normally, through an anti-bacterial filter while wearing a nose clip, holding their head in a slightly chin-up position and supporting their own cheeks. After a period of breathing stabilisation, three 30-s recordings of tidal breathing were made with the operator monitoring the subject's head position, and measurements for leaks, swallows or cough. Three maximal deep inspiratory breaths were performed in the seated position from which IC was calculated. Subjects were moved into the supine position, supported with one pillow under their head. In the supine posture the same neutral neck position was maintained with the operator holding the device in position and tidal breathing and IC breaths were again recorded.

Trials containing artifacts were excluded and measurements repeated. Measurements were assessed off-line for quality (M. Srinivasan). Any breaths containing resistances that were negative or were >5 standard deviations above the mean were excluded. Supine persistent hyperinflation was measured by the change in seated to supine IC and the supine IC/TLC ratio. There are no agreed upon criteria to define the presence of supine persistent hyperinflation. In our study, the within-subject variability when measuring IC was approximately 200 mL. We have, therefore, used this as a cut-off for defining supine persistent hyperinflation. TremoFlo (version 1.0.44.40, 2019) was used for offline analysis of data and data export.

We report only the impedance results for 5 Hz. The mean R_{rs} and X_{rs} of each acquisition was calculated, from which the mean of the three recordings were calculated ($R_{rs\text{mean}}$ and $X_{rs\text{mean}}$). We also calculated R_{rs} and X_{rs} of expiration and inspiration separately and calculated the difference between the mean inspiratory and expiratory X_{rs} (ΔX_{rs}), as the mean of all inspiratory X_{rs} in the acquisition, minus the mean of all expiratory X_{rs} , then calculating the mean difference of the three acquisitions. This method is slightly different to the technique described by DELLACÀ *et al.* [18] where within-breath differences in inspiratory and expiratory X_{rs} were calculated. Due to technical difficulties, we were unable to calculate intra-breath differences and given both methods yield similar results, we proceeded to use the threshold value of $\Delta X_{rs} \geq 2.8 \text{ cmH}_2\text{O}\cdot\text{L}^{-1}\cdot\text{s}^{-1}$ during tidal volume breathing indicating that significant EFL was present [18]. This value has been demonstrated to accurately predict flow limitation in COPD in both the seated and supine position [16]. All pulmonary function and oscillometry parameters were expressed as z-scores, using Global Lung Function Initiative equations for spirometry [21] and lung volumes [22], QUANJER *et al.* [23] for FRC/TLC and OOSTVEEN *et al.* [24] for oscillometry.

Statistical analysis

Prior research has reported a mean IC change between the seated and supine position of approximately 400 mL in healthy subjects [11]. It was therefore estimated that at least 27 COPD patients were required at 80% power to detect a change in IC of 400 mL, type 1 error 0.05.

The only published data on supine change in ΔX_{rs} was by MILESI *et al.* [25] which showed a small change of $0.74 \text{ cmH}_2\text{O}\cdot\text{s}^{-1}\cdot\text{L}^{-1}$. This was measured with the patients using a continuous positive airway pressure (CPAP) mask which influenced the results. In our pilot studies we found a mean \pm SD change in ΔX_{rs} seated to supine of $2.5\pm 3.4 \text{ cmH}_2\text{O}\cdot\text{s}^{-1}\cdot\text{L}^{-1}$. This led to a sample size calculation of 41 patients with a power of 80%, type 1 error 0.05. There is no published data on the relationship between the change in ΔX_{rs} and change in IC. We anticipated a linear correlation coefficient of around 0.4 to arrive at a sample size of 41 with a power of 80%, type 1 error 0.05.

Data was analysed using Jamovi 2.3.28 and SPSS statistics. Graphs were generated through GraphPad Prism version 10.2.2. Data are presented as mean \pm SD or median (interquartile range) as appropriate. Paired samples t-test was performed to analyse differences in oscillometry parameters and IC between the seated and supine positions. The association between supine hyperinflation and baseline anthropomorphic and spirometric parameters was measured by Spearman's correlation due to not normally distributed data. A p-value of <0.05 was considered statistically significant.

Results

42 stable COPD patients without relevant comorbidities and 14 healthy controls were enrolled in the study. Anthropomorphic and clinical data of the two groups is shown in tables 1 and 2. COPD subjects were slightly older but with similar body mass index (BMI) and sex distribution. COPD patients had moderately severe airflow obstruction and mild baseline gas trapping (increased residual volume/total lung capacity, RV/TLC) and hyperinflation (FRC/TLC) compared with controls. There was mild impairment of

TABLE 1 Baseline characteristics

	COPD (n=42)	Control (n=14)	p-value
Anthropometric data			
Age (years)	68.5±9.1	60.8±9.5	0.009
Female sex (%)	45.24	57.14	0.44
BMI (kg·m ⁻²)	26.3±4.9	25.9±3.6	0.76
Spirometry and lung volumes			
FEV ₁ (L)	1.46±0.58	3.10±0.97	<0.001
FEV ₁ (Z-score)	-2.67±1.17	0.23±1.10	<0.001
FVC (L)	3.07±0.85	4.10±1.19	<0.001
FVC (Z-score)	-0.72±1.14	0.44±1.04	0.002
FEV ₁ /FVC	47.1±12.5	75.5±5.05	<0.001
FEV ₁ /FVC (Z-score)	-3.28±1.07	-0.39±0.68	<0.001
TLC (L)	6.26±1.17	6.39±1.35	0.728
TLC (Z-score)	0.58±1.03 [#]	-0.37±1.04	0.52
FRC (Z-score)	1.68±1.15 [#]	0.56±0.95	0.002
FRC/TLC (Z-score)	1.29±1.45 [#]	-0.05±1.52	0.005
RV (Z-score)	1.53±1.01 [#]	0.42±1.02	0.001
RV/TLC (Z-score)	1.86±1.15 [#]	0.48±1.19	<0.001

Values are presented as mean±SD, unless otherwise stated. **Bold** indicates statistical significance. BMI: body mass index; FEV₁: forced expiratory volume in 1 s; FVC: forced vital capacity; TLC: total lung capacity; FRC: forced residual capacity; RV: residual volume. #: data missing for 1 patient.

respiratory resistance at 5 Hz (R_{rs5}) but severely reduced respiratory reactance at 5 Hz (X_{rs5}) while values in the control group were within normal limits (see table 2).

The changes in IC/TLC, R_{rs} and X_{rs} with supine posture are shown in table 3. COPD subjects demonstrated supine persistent hyperinflation with no change in IC/TLC from seated to supine posture ($p=0.08$). In contrast, the control subjects showed a significant increase in IC ($p<0.001$) and in IC/TLC ($p=0.0005$) (see figure 1). Dynamic elastance (X_{rs5}) became more negative in supine posture in both cohorts ($p<0.001$ for both healthy and COPD, see table 3) with no difference between groups in the change ($p=0.152$). There was also a significant increase in ΔX_{rs5} between seated and supine posture in COPD patients ($p<0.001$), such that the number of subjects with $\Delta X_{rs5} > 2.8 \text{ cmH}_2\text{O}\cdot\text{L}^{-1}\cdot\text{s}^{-1}$ (the cut-off used for indicating the presence of airways closure) increased from 15 out of 42 (35.7%) to 27 out of 42 (64.3%). Although a statistically significant increase in the ΔX_{rs5} was also seen in controls in supine posture ($p=0.039$), only one healthy subject had a ΔX_{rs5} of $> 2.8 \text{ cmH}_2\text{O}\cdot\text{L}^{-1}\cdot\text{s}^{-1}$ in the supine position (see figure 2). Using the cut-off value of an increase in supine IC of 200 mL, 31/41 (75.6%) patients and 5/14 (35.7%) controls demonstrated supine persistent hyperinflation. There is a possible sex difference as shown in supplementary tables 1 and 2 but strong conclusions could not be drawn.

The univariate predictors of supine IC/TLC (hyperinflation) are shown in table 4. In control subjects, RV/TLC Z-score was the sole predictor of supine IC/TLC. In the COPD cohort, the predictors of worse supine

TABLE 2 Baseline oscillometry characteristics

	COPD (n=42)	Control (n=14)	p-value
Seated R_{rs5} (cmH ₂ O·L ⁻¹ ·s ⁻¹)	4.88 (3.77–6.67)	2.71 (2.42–3.67)	<0.001
Seated R_{rs5} (Z-score)	1.59±1.73	-0.01±0.87	<0.001
Supine R_{rs5} (cmH ₂ O·L ⁻¹ ·s ⁻¹)	6.4 (4.62–8.28)	3.82 (3.35–5.25)	0.005
Supine R_{rs5} (Z-score)	2.54±1.35	1.39±0.7	0.003
Seated X_{rs5} (cmH ₂ O·L ⁻¹ ·s ⁻¹)	-3.27 (-5.21– -2.32)	-1.26 (-1.59– -0.84)	<0.001
Seated X_{rs5} (Z-score)	-4.62±3.77	-0.04±1.15	<0.001
Supine X_{rs5} (cmH ₂ O·L ⁻¹ ·s ⁻¹)	-6.04 (-8.12– -3.75)	-1.61 (-3.06– -1.37)	<0.001
Supine X_{rs5} (Z-score)	-7.72±3.91	-2.17±1.77	<0.001
Seated ΔX_{rs5} (cmH ₂ O·L ⁻¹ ·s ⁻¹)	1.59 (0.42–3.59)	-0.14 (-0.30–0.04)	0.001

Values are mean±SD or median (interquartile range). **Bold** indicates statistical significance. R_{rs5} : respiratory resistance at 5 Hz; X_{rs5} : respiratory reactance at 5 Hz; ΔX_{rs5} : difference between inspiratory and expiratory reactance.

TABLE 3 Seated versus supine parameters

	COPD (n=42)		p-value	Control (n=14)		p-value
	Seated	Supine		Seated	Supine	
IC (L)	1.94±0.67 [#]	1.99±0.68 [#]	0.12	2.42±0.91	2.89±1.1	<0.001
IC/TLC	0.31±0.09 [#]	0.32±0.09 [#]	0.079	0.37±0.07	0.44±0.09	<0.001
ΔX_{rs} (cmH ₂ O·L ⁻¹ ·s ⁻¹)	2.28±2.55	4.91±4.10	<0.001	-0.12±0.46	0.51±1.27	0.039
R_{rs5} (Z-score)	1.59±1.73	2.54±1.35	<0.001	-0.1±0.86	1.39±0.70	<0.001
X_{rs5} (Z-score)	-4.62±3.77	-7.72±3.91	<0.001	-0.04±1.15	-2.17±1.77	<0.001

Values are mean±sd. **Bold** indicates statistical significance. IC: inspiratory capacity; TLC: total lung capacity; R_{rs5} : respiratory resistance at 5 Hz; X_{rs5} : respiratory reactance at 5 Hz; ΔX_{rs5} : difference between inspiratory and expiratory reactance. [#]: data missing for 1 patient.

hyperinflation were older age, lower BMI, worse airflow obstruction and closure, according to FEV₁/FVC, RV/TLC, X_{rs5} and ΔX_{rs5} . In multivariate analyses examining the effects of oscillometry parameters (see figure 3), age, BMI and X_{rs5} Z-score were independent predictors of supine IC/TLC accounting for 39% of the variability ($p < 0.001$, standardised β coefficients -0.226, 0.457, 0.464, respectively). Using ΔX_{rs} instead of X_{rs} Z-score produced similar results and accounted for 29% of the variability in IC/TLC ratio ($p = 0.001$, standardised β coefficients -0.282, 0.311 and -0.321, respectively).

In both control subjects and COPD patients, there were no associations between changes in any oscillatory impedance or spirometric parameters; and the changes in IC/TLC between seated to supine postures (see table 4).

Discussion

This is the first prospective, observational study to determine the relationship between supine persistent hyperinflation in COPD and dynamic elastance and tidal expiratory flow limitation. Patients with COPD exhibit supine persistent hyperinflation whereas healthy controls do not. In healthy subjects there was an increase in IC/TLC ratio when supine due to the aforementioned reduction in supine FRC with no change to TLC, resulting in an increase in IC. In healthy individuals there were also increases in R_{rs5} and ΔX_{rs5} , and a decrease in X_{rs5} (worsening dynamic elastance). The changes in R_{rs5} , ΔX_{rs5} and X_{rs5} were, however, independent of volume changes occurring due to an increase in IC/TLC. In contrast in the COPD patients, IC/TLC did not change between seated and supine posture, strongly suggesting that they exhibited relative supine hyperinflation. Despite this, there were also increases in R_{rs5} and ΔX_{rs5} , and X_{rs5} became more

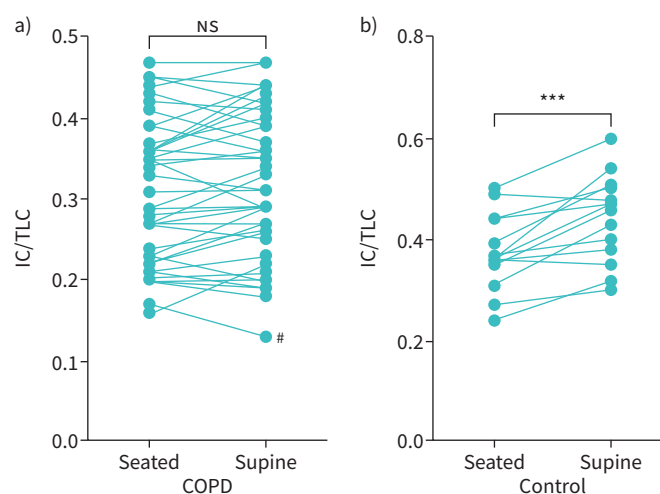


FIGURE 1 Inspiratory capacity/total lung capacity ratios (IC/TLC), in upright and supine postures for (a) COPD cohort (n=41, $p=0.0759$) and (b) control subjects (n=14, $***: p=0.0005$). [#]: Technical difficulties with exporting this subject's data may have affected results obtained. Analysis was run with and without this patient included in the dataset with no change to results. NS: not statistically significant.

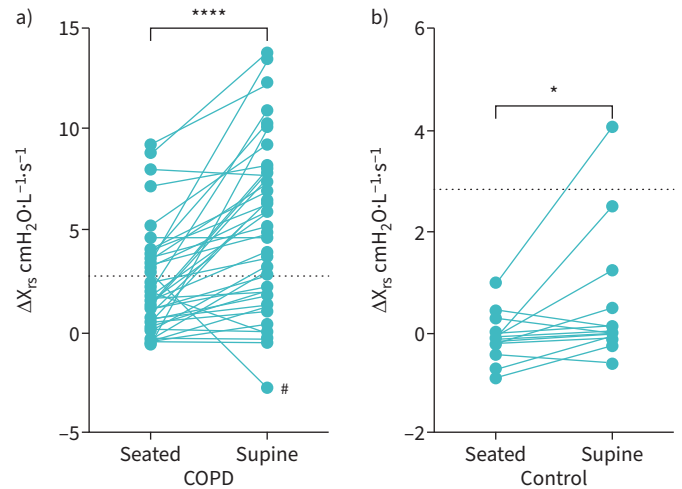


FIGURE 2 Difference between inspiratory and expiratory reactance (ΔX_{rs}) in the seated and supine position for COPD patients (panel a, n=42, p<0.0001) and control subjects (panel b, n=14, p=0.0388). Dotted line at ΔX_{rs5} 2.8 cmH₂O·L⁻¹·s⁻¹, signifying significant expiratory flow limitation. #: Technical difficulties with exporting this subject's data may have affected results obtained. Analysis was run with and without this patient included in the dataset with no change to results.

negative. The independent predictors of greater hyperinflation (IC/TLC) in COPD patients, were older age, lower BMI and worse ventilatory impairment as indicated by either upright spirometry or X_{rs5} . Lastly, as is shown in table 4, the changes in oscillatory impedance due to supine posture were unrelated to IC and

TABLE 4 Univariate correlations between anthropomorphic, spirometric and oscillometry parameters and supine hyperinflation as measured by supine IC/TLC ratio and the change in IC/TLC from the seated to supine position

	COPD (n=41)				Control (n=14)			
	Supine IC/TLC [#]		Change in IC/TLC		Supine IC/TLC		Change in IC/TLC	
	r _s	p-value	r _s	p-value	r _s	p-value	r _s	p-value
Age (years)	0.321	0.041	0.096	0.545	-0.17	0.562	-0.099	0.736
BMI (kg·m ⁻²)	0.341	0.029	0.061	0.704	0.420	0.137	0.127	0.664
FEV ₁ (L)	0.674	<0.001	0.254	0.104	0.429	0.126	0.597	0.048
FEV ₁ (Z-score)	0.587	<0.001	0.090	0.575	0.437	0.118	0.358	0.208
FEV ₁ /FVC	0.603	<0.001	0.266	0.08	0.178	0.542	0.180	0.537
FEV ₁ /FVC (Z-score)	0.504	0.001	0.012	0.939	0.0284	0.326	0.442	0.114
RV/TLC	-0.803	<0.001	-0.11	0.495	-0.899	<0.001	-0.614	0.02
RV/TLC (Z-score)	-0.557	<0.001	-0.201	0.221	-0.824	<0.001	-0.424	0.131
R _{rs5} (cmH ₂ O·L ⁻¹ ·s ⁻¹)	-0.227	0.153	-0.245	0.118	0.407	0.15	-0.042	0.887
R _{rs5} (Z-score)	-0.282	0.074	0.014	0.930	-0.169	0.563	-0.367	0.197
X _{rs5} (cmH ₂ O·L ⁻¹ ·s ⁻¹)	0.499	0.001	0.268	0.086	0.0857	0.773	0.460	0.098
X _{rs5} (Z-score)	0.405	0.009	-0.090	0.578	0.424	0.131	0.073	0.805
ΔX_{rs5} (cmH ₂ O·L ⁻¹ ·s ⁻¹)	-0.413	0.007	-0.18	0.252	-0.275	0.341	0.398	0.158
Supine ΔX_{rs5} (cmH ₂ O·L ⁻¹ ·s ⁻¹)	-0.465	0.002	-0.239	0.127	-0.279	0.333	0.0484	0.869
Change in R _{rs5}	-0.091	0.574	0.17	0.274	0.35	0.22	0.396	0.16
Change in X _{rs5}	0.107	0.505	0.02	0.899	-0.231	0.427	0.022	0.94

Bold indicates statistical significance. r_s: Spearman correlation coefficient; R_{rs5}: respiratory resistance at 5 Hz; X_{rs5}: respiratory reactance at 5 Hz; ΔX_{rs5} : difference between inspiratory and expiratory reactance during tidal volume breathing; change in R_{rs5} and X_{rs5}: changes in Z-scores between upright and supine posture; IC: inspiratory capacity; TLC: total lung capacity; BMI: body mass index; FEV₁: forced expiratory volume in 1 s; FVC: forced vital capacity; RV: residual volume. #: in the COPD cohort, there was little difference between mean seated and supine IC/TLC and therefore similar relationships were seen in the seated parameter.

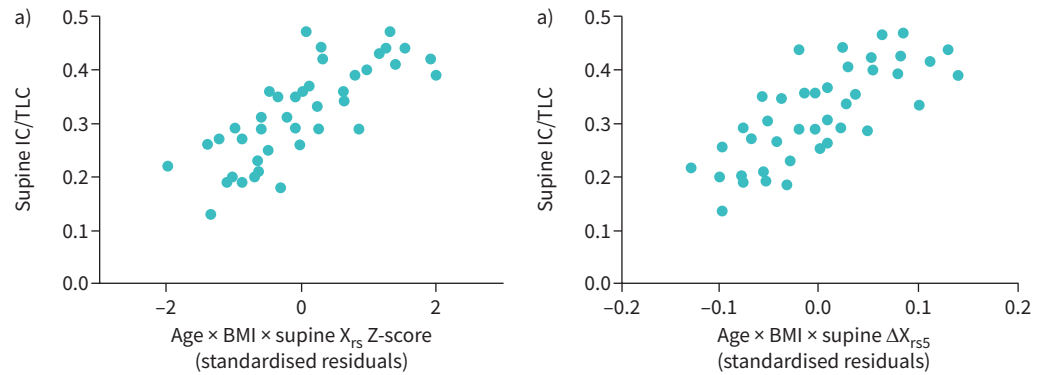


FIGURE 3 Predictors of supine hyperinflation (supine inspiratory capacity/total lung capacity ratios; IC/TLC). **a)** COPD cohort; x-axis shows standardised residuals of regression with age (years), body mass index (BMI, $\text{kg}\cdot\text{m}^{-2}$) and supine respiratory reactance (X_{rs} , Z-score) as predictors ($n=41$, adjusted $r^2=0.39$, $p<0.001$, standardised β coefficients -0.226 , 0.457 , 0.464 , respectively). **b)** COPD cohort; x-axis shows standardised residuals of regression with age (years), BMI ($\text{kg}\cdot\text{m}^{-2}$) and the supine difference between inspiratory and expiratory reactance (ΔX_{rs5} $\text{cm H}_2\text{O}\cdot\text{L}^{-1}\cdot\text{s}^{-1}$) as predictors ($n=41$, adjusted $r^2=0.39$, $p=0.001$, standardised β coefficients -0.229 , 0.404 and -0.459 , respectively).

therefore independent of changes in operating lung volume in both healthy controls and COPD patients and are presumably due to changes in the distribution and overall magnitude of regional time constants.

In healthy subjects, FRC and therefore end-expiratory lung volume (EELV) decrease with supine posture, which has been shown to partially explain increases in R_{rs} and decreases in X_{rs} [26]. Changes in EELV with supine posture, as measured by ERV (since RV and TLC change minimally [26–28]), are less with older age [29] and obesity [30]. In upright posture, R_{rs} and X_{rs} are both strongly volume dependent [31–33]. Airway closure causes reactance to suddenly decrease. In the supine position, the fall in FRC means that airway closure may occur during tidal volume breathing due to FRC falling below closing capacity.

The location of closure also changes, being in dependent lung regions in healthy subjects [34] and so in supine posture, will change from caudal regions to being along the posterior regions of the lung. The distribution of airway calibres will also change. Hence the effects of supine posture on R_{rs} and X_{rs} are a complex interaction of changes in lung volume, distributions of compliances and airway calibres, airway closure, age and BMI. Emphysema is a heterogenous disease, and the size and location of bullous disease may further impact on changes in respiratory mechanics when patients are moved into the supine position. Assessing the impact of the heterogenous distribution of emphysema was outside the scope of this study but would be an interesting direction for further research.

In the current study, the changes in supine oscillometry parameters were not correlated with changes in EELV, again suggesting that the supine increase in R_{rs} and ΔX_{rs} and decrease in X_{rs} cannot be attributed to a change in volume alone. The strong relationship between supine IC/TLC and RV/TLC in healthy subjects is expected given that for IC to increase, EELV gets closer to RV *i.e.* if RV/TLC is high, it would inhibit any increase in IC/TLC, given RV/TLC does not change in supine posture.

ELBEHAIRY *et al.* [11] previously demonstrated the lack of supine IC change in patients with severe COPD. Worsening of R_{rs} and X_{rs} in the supine posture [11, 25], has also previously been demonstrated but the relationship between supine persistent hyperinflation with upright and supine oscillatory mechanics and anthropomorphic factors, has not been previously reported. These findings suggest that the drivers of supine EELV in COPD are predominantly airway closure and expiratory flow limitation. We found ΔX_{rs5} to be the strongest oscillometric driver of supine IC/TLC, while R_{rs5} was not, which supports this proposed mechanism of supine persistent hyperinflation in COPD. We postulate that the overall worsening of ventilatory function while supine is a consequence of the gravitational effects on the lungs in COPD, which may lead to a reduction in mean airway calibre, increased airway closure and more EFL and that the consequence of this is maintenance of hyperinflation. Maintenance of hyperinflation may mitigate these effects on the work of breathing and perhaps also on gas exchange. Higher ΔX_{rs5} indicates a larger increase in dynamic elastance in expiration, due to increasing airway collapse, to the point of expiratory flow

limitation. DELLACÀ *et al.* showed that when ΔX_{rs5} exceeded $2.8 \text{ cmH}_2\text{O}\cdot\text{L}^{-1}\cdot\text{s}^{-1}$, this predicted a flow-limited breath [18]. The linear relationship between ΔX_{rs5} and supine IC/TLC (see figure 3b) suggests that even values which do not reach this threshold may have a physiological effect on EELV.

In addition to ΔX_{rs} , BMI was also an independent predictor of supine persistent hyperinflation in COPD. While larger ΔX_{rs} was associated with more supine hyperinflation, higher BMI was associated with less supine hyperinflation. Higher BMI is associated with less resting hyperinflation in COPD, greater maximal oxygen consumption and less breathlessness at any given minute of ventilation [35]. Thus, the effects of obesity in reducing static hyperinflation may explain part of the “obesity paradox”. Our data also suggest that higher BMI mitigates to some extent, the effects of ventilatory impairment (ΔX_{rs5}) on persistent supine hyperinflation. We note that the effects of BMI on supine hyperinflation in our COPD participants, only apply to mild obesity, since the maximum BMI was $36.6 \text{ kg}\cdot\text{m}^{-2}$.

Understanding the physiologic changes that occur in COPD patients in the supine position is clinically important since nocturnal symptoms are common in COPD [7, 10, 11]. Clinicians are aware that supine breathlessness, nocturnal symptoms and sleep disturbance may be due to comorbidities such as heart failure and obstructive sleep apnoea. Ironically there is much less appreciation of how those symptoms may be due to an increase in hyperinflation, airflow obstruction and expiratory flow limitation. Supine persistent hyperinflation is likely driven by expiratory flow limitation, airway closure and intrinsic positive end expiratory pressure. It is hypothesised that COPD patients maintain hyperinflation to minimise the effects of airway collapse and closure, thereby reducing the resistive work of breathing. The disadvantage to this is the resulting, higher mean trans-respiratory pressures and the requirement of larger pressure swings to generate the same change in volume, and thus greater elastic cost to the work of breathing and perhaps greater symptoms. Supine EFL and hyperinflation are likely to impact sleep quality and strategies to optimise respiratory mechanics during sleep might provide clinical benefit.

This study has some limitations. Firstly, TLC was not measured in the supine position and some studies have demonstrated small but statistically significant reductions in TLC in the supine position. Thus, the assumption that changes in IC reflect changes in EELV may not be entirely valid [26, 27, 36]. Secondly, the control group was small and on average, 8 years younger than the patient group. This made interpreting the effect of anthropomorphic factors in this group difficult. A larger study of healthy subjects of wider range of BMI and age, would be useful to better understand what represents “normal” supine oscillometry. Similarly, the mean age of patients from the the reference dataset used by OOSTVEEN *et al.* [24] was approximately 50 years which may affect the standardisation of data in both the COPD and control population.

In conclusion, supine persistent hyperinflation occurs in COPD but not in healthy participants and is associated with increased dynamic elastance and EFL, likely the result of increased airway closure due to gravitational redistribution of lung mass in the supine posture. This effect is modified by age and BMI. While healthy participants demonstrate both a decrease in supine EELV and worsening of oscillometric parameters, they are dissociated, suggesting that there is a complex interplay of factors including weight, age, changes in lung volume and airway closure. Further studies assessing the relationships between supine hyperinflation and EFL; and daytime and nocturnal symptoms and polysomnographic parameters in COPD are warranted to determine if there may be clinical benefit from targeting supine hyperinflation and EFL.

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Conflict of interest: G.G. King is a nonexecutive board member of Cyclomedica Ltd, Australia. He has received honoraria for consultancy services to AstraZeneca, Chiesi, GSK, Sanofi. He receives grants from Cyclomedica and philanthropic trusts. All other authors have nothing to disclose.

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