# Dynamic compliance and reactance in older non-smokers with asthma and fixed airflow obstruction



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*To the Editor:*

In asthma, abnormal mechanical properties of the airways and lung tissue leads to airway narrowing and changes in ventilation distribution [1]. Ventilation distribution is determined by the variation of time constants [2], the product of resistance and static compliance of individual lung units. Ventilation distribution is heterogeneous in healthy lungs, but even more so in airway diseases, including asthma [3]. This is because time constants are often even more heterogeneous in disease due to changes in resistances and compliances [3, 4]. Lung compliance measured under dynamic conditions, *e.g.* during breathing (dynamic compliance, or $C_{dyn}$), is sensitive to these heterogeneities in time constants. $C_{dyn}$ decreases relative to static compliance ($C_{stat}$) with increasing ventilation heterogeneity [2, 3, 5], due to diversion of ventilation from lung units with longer to those with shorter time constants [6]. Hence $C_{dyn}$ is a measure of lung function in relation to ventilation heterogeneity under tidal breathing conditions, that complements spirometry. However, $C_{dyn}$ is not used clinically because it requires invasive oesophageal pressure measurements.

The forced oscillation technique, also known as oscillometry, provides another measure of dynamic compliance. Oscillometry is a method of measuring respiratory system mechanics, which includes mechanics of the chest wall, lung and airways. Pressure oscillations (typically frequencies between 5 and 19 Hz) that are higher than typical breathing rates are imposed at the airway opening during normal, relaxed breathing [7]. During oscillometry measurements, the relationship between pressure change and resultant airflow allow both respiratory system resistance ($R_{rs}$) and reactance ($X_{rs}$) to be derived. Oscillometry measurements at low frequency, being physiologically and clinically important, are commonly made at around 5 Hz. $X_{rs}$ has compliance and inertial components but at low frequencies, is dominated by compliance with little contribution from inertance. The lower the compliance, the more negative $X_{rs}$. Similar to $C_{dyn}$, modelling studies suggest that compliance measured *via* oscillometry is highly sensitive to heterogeneity in time constants [5]. $C_{dyn}$ and oscillometry are measured at different frequencies, which can account for the variation in measurements. However, there is a degree of physical similarity between $C_{dyn}$ and oscillometry because of the way in which they are derived. During breathing a person generates their own flow and compliance is measured at the peaks and troughs of volume (*i.e.* at zero flow). During oscillometry measurement, flows are generated externally, and compliance is derived from the "out of phase" flow (*i.e.* during the peaks and trough of flow oscillation at zero pressure). Thus, $X_{rs}$ should be related to $C_{dyn}$ of the lung, with lower dynamic compliance (represented by lower, more negative $X_{rs}$) correlating with lower $C_{dyn}$. Having experimental data confirming this theoretical relationship in asthma would strongly inform clinical interpretation of $X_{rs}$ in this condition.

Therefore, the aim of this study was to assess relationships between $X_{rs}$ at 5 Hz ($X_5$), static ($C_{stat}$) and dynamic ($C_{dyn}$) lung compliance in non-smokers with asthma and fixed, non-reversible airflow obstruction (FAO). These individuals typically have more negative $X_{rs}$, increased $C_{stat}$ and increased ventilation heterogeneity [1]. We hypothesised that in this cohort, $X_5$ relates to $C_{dyn}$ rather than to $C_{stat}$ at resting and higher breathing rates. $C_{stat}$ and $X_5$ data from this cohort have been previously published [4], however the $C_{dyn}$ data and its relationships with $C_{stat}$ and $X_5$ are novel.

Shareable abstract (@ERSpublications)
**In older non-smokers with asthma and fixed airflow obstruction, $X_5$ measured by oscillometry reflects dynamic rather than static compliance. Distinguishing between dynamic and static compliance is important as they are due to different factors.** https://bit.ly/3th0uEr

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We enrolled participants from tertiary hospital clinics who were >40 years old, had ⩽5 pack-years smoking history and a physician-diagnosis of asthma [4]. To minimise inflammation, all participants were treated with 2 months of maximal dose inhaled corticosteroid/long-acting beta-agonist (ICS/LABA) using a fluticasone/eformoterol 250 µg/10 µg metered dose inhaler, two puffs twice daily. At the end of the 2-month treatment, participants performed standard lung function tests according to European Respiratory Society/American Thoracic Society standards [8, 9]. Oscillometry was performed as previously described [4]; $R_5$ and $X_5$ were expressed as z-scores [10]. $C_{stat}$ was measured using oesophageal manometry as previously described [4]. In brief, the static pressure–volume (P–V) curve was constructed from points obtained during at least five interrupted deflation manoeuvres from total lung capacity to functional residual capacity (FRC) [1]. $C_{stat}$ was calculated as the slope of the deflation static P–V curve between FRC and FRC +1 L [11]. $C_{dyn}$ was measured at breathing frequencies of 15, 30 and 60 breaths·min$^{-1}$ (bpm), and calculated by dividing the volume change by the pressure change, between the points of zero flow at end-inspiration and at end-expiration. The average of a minimum of 10 breaths at each breathing rate was used. Ethics approval was granted by the Sydney Local Health District Human Research Ethics Committee (HREC/14/CRGH/75).

Correlations between $X_5$ and $C_{stat}$ and $C_{dyn}$ were assessed using Spearman's rank test. The transformation to $-1/X_5$ was used since it is linearly (and positively) proportional to compliance [12, 13]. All data were analysed using SPSS Statistics v26 (IBM, Armonk, NY, USA).

18 participants with asthma (mean±SD age 64.1±8.0 years) were enrolled. All were taking ICS±LABA. Mean forced expiratory volume in 1 s/forced vital capacity ($FEV_1$/FVC) z-score was −2.6±0.7. There was moderate to severe impairment of impedances, with median (interquartile range) $R_5$ and $X_5$ z-scores of 2.7 (1.9–3.2) and −4.1 (−7.3–2.4), respectively. $C_{stat}$ median (interquartile range) was 0.221 (0.177–0.287) L·cm$H_2O^{-1}$. $C_{dyn}$ was frequency dependent, being significantly less with increasing breathing frequency: 0.094 (0.067–0.125) L·cm$H_2O^{-1}$ at 15 bpm, 0.052 (0.047–0.065) L·cm$H_2O^{-1}$ at 30 bpm and 0.037 (0.028–0.044) L·cm$H_2O^{-1}$ at 60 bpm (p<0.0001). $C_{dyn}$ expressed as a % of $C_{stat}$ at each breathing frequency (normal cut off defined as ⩾80%) [3] were 39% (30–69%), 22% (16–33%) and 15% (10–34%), respectively, and differed significantly from each other (p=0.001).

Reactance (expressed as $-1/X_5$) was unrelated to $C_{stat}$ (p=0.2) but was related to $C_{dyn}$ at all breathing frequencies ($r_s$=0.72, p=0.001 at 15 bpm; $r_s$=0.79, p<0.0001 at 30 bpm; and $r_s$=0.60, p=0.009 at 60 bpm) (figure 1). $C_{dyn}/C_{stat}$ ratio, however, was not related to $-1/X_5$ (p=0.09, p=0.25 and p=0.62, respectively). $C_{dyn}$ and $C_{dyn}/C_{stat}$ at all breathing rates and $-1/X_5$ were all unrelated to $FEV_1$/FVC or $FEV_1$/FVC z-score (p⩾0.10). Increasing breathing rates were associated with increasing FRC. Mean±SD FRC was 3.89±1.09 L, 4.14±1.08 L and 4.49±1.08 L at 15, 30 and 60 bpm, respectively (p<0.001). Differing FRCs however, were unrelated to $C_{dyn}$ (p⩾0.30).

In summary, in this cohort of older non-smokers with asthma and FAO, we confirmed theoretical predictions that $X_5$ is a marker of $C_{dyn}$ rather than of $C_{stat}$. As such, $X_5$ is a marker of ventilation heterogeneity, which was present in these asthmatic participants with FAO.

Our findings are consistent with those of Oppenheimer *et al.* [14], who also demonstrated a correlation between $X_5$ and $C_{dyn}$ at 60 bpm, and similarly an absence of correlation between $X_5$ and $C_{stat}$. They reported results only at 60 bpm and so it is uncertain if this relationship was also present at lower breathing rates that we reported. The participants in their study were younger than in our study, had a variety of respiratory symptoms and diagnoses, but normal spirometry [14]. Because of FAO in our subjects, $C_{dyn}$ was reduced even at low breathing rates, consistent with worse ventilation heterogeneity, which may have allowed us to see relationships at lower breathing rates.

While at the low breathing rates $C_{dyn}$ is brought closer to $C_{stat}$, indicating the presence of slowly ventilating lung units, the $C_{dyn}/C_{stat}$ ratio was not related to $X_5$. This may be surprising given the correlation between $C_{dyn}$ and $X_5$. However, it may suggest that at the breathing rates studied, the contribution to both $C_{dyn}$ and $X_5$ from heterogeneity in time constants within the lung is greater compared to the contribution from the overall elastic properties of the chest wall and lung (which are the main determinants of $C_{stat}$). It would also explain why $C_{stat}$ is poorly correlated with $X_5$.

Dynamic hyperinflation occurred with increasing breathing rates. This is not surprising given the presence of FAO in many of the participants. However, increasing FRC was unrelated to $C_{dyn}$. Interestingly, both $-1/X_5$ and $C_{dyn}$ were unrelated to spirometric obstruction, suggesting that physiological and clinical significances of dynamic compliance and spirometry may be independent.

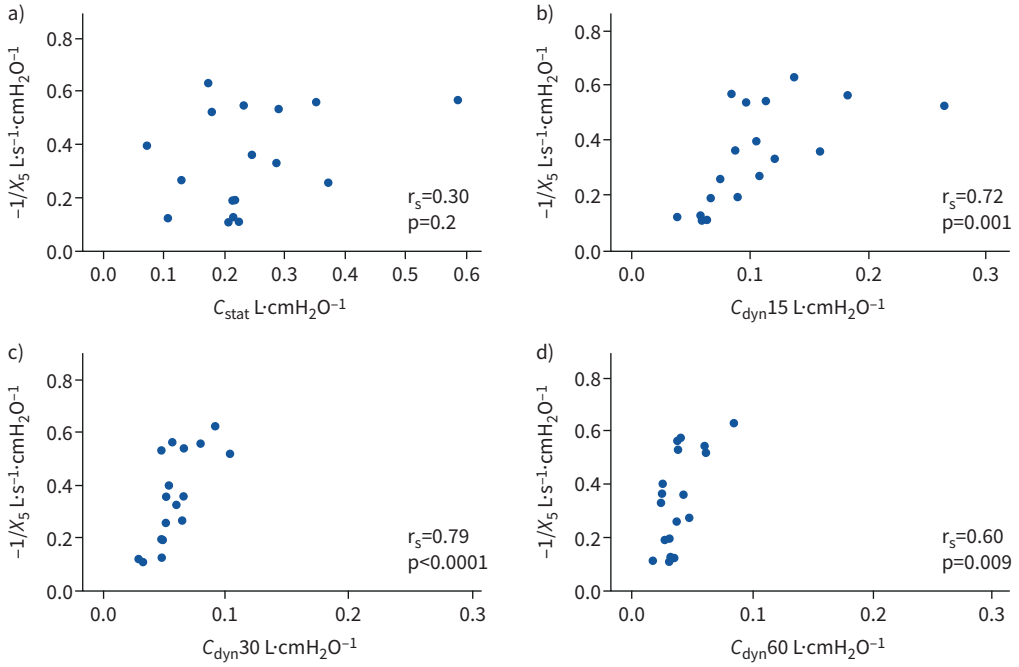


**FIGURE 1** Correlations between $-1/X_5$ and a) static compliance ($C_{stat}$), and dynamic compliance at b) 15 breaths·min$^{-1}$ ($C_{dyn}$15), c) 30 breaths·min$^{-1}$ ($C_{dyn}$30) and d) 60 breaths·min$^{-1}$ ($C_{dyn}$60).

In conclusion, $X_5$ measured by oscillometry reflects dynamic compliance during spontaneous breathing in non-smokers with asthma and FAO. $X_5$ is commonly thought to reflect the elastic properties of the respiratory system, assumed to be its static properties. Our findings show that in asthma with FAO, $X_5$ reflects dynamic rather than static compliance. It is important to distinguish between static and dynamic compliance, because they reflect different determinants and, therefore, have different clinical implications. Thus, our findings suggest that $X_5$ is sensitive to heterogeneous time constants, an important functional abnormality in asthma. This physiological relationship aids clinical interpretation of oscillometry measurements in asthma and supports its use as a clinically useful parameter in practice and airways research.

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This study is registered at www.anzctr.org.au with identifier number ACTRN12615000985583. The data sets generated and/or analysed during the study are available from the corresponding author on reasonable request.

Conflict of interest: T. Durack has nothing to disclose. D.G. Chapman has nothing to disclose. S. Rutting has nothing to disclose. C. Thamrin has a patent WO 2006130922 A1 issued which is broadly relevant to the work; and has intellectual property arrangements with Thorasys Medical Systems and Restech srl relating to research collaborations, but does not have any financial relationships with either company. G.G. King reports grants from University of Sydney Bridging Grant, during the conduct of the study; grants, personal fees for consultancy,

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