Assessment of lung function in patients with COPD using the Inspired Sinewave Technique

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Introduction

The Inspired Sinewave Technique (IST) is a novel method for measuring parameters of cardiopulmonary function – Lung volume, pulmonary blood flow and indices of ventilatory heterogeneity.

It requires only passive cooperation from patients and minimal operator skill/experience. As such the technology can provide simple non-invasive measurements for patients in critical care settings, as well as out patients.

Aims:

As ventilatory heterogeneity (VH) increases with normal ageing[1] and obstructive lung disease[2] we aim to assess:

1. The age dependency of the IST indices of VH
2. The diagnostic value of the IST test for COPD, and its ability to stage patients based upon the GOLD classification of airflow imitation severity[3]

The Inspired Sinewave Technique (IST)

Over successive tidal breaths the concentration of a tracer gas in patients inspired air (nitrous oxide, N_2O) is sinusoidally oscillated around a set mean (4%) with a pre-determined amplitude (3%) and frequency (60sec or 180sec period).

The amplitude & phase of the expired sinewave is altered by pulmonary ventilation and blood flow (if the tracer gas is soluble) and distorted further by VH (fig 1).

Using a single-compartment tidal ventilation lung model, the resulting amplitude/phase of the expired sinewave allows the estimation of[4,5]:

- Equivalent lung volume (ELV)
- Pulmonary blood flow (Q_P)
- Ventilation heterogeneity (VH)

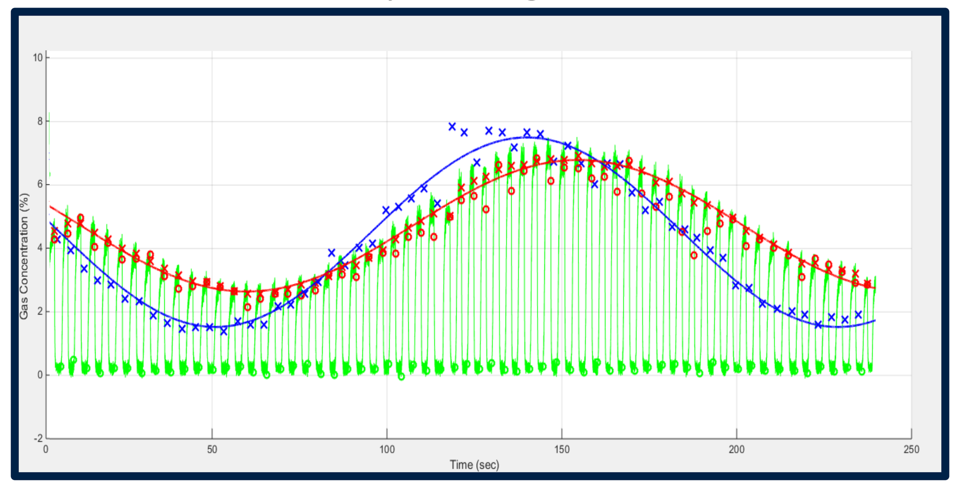

Figure 1 *A typical data set collected from one participant. –, expired N_2O concentration; x and x, N_2O concentrations in inspired gas and end-tidal gas respectively; – and –, inspired and expired N_2O sinewaves respectively.*

VH Indices

A) ELV/FRC_{pleth}
B) ELV_{60}/ELV_{180}

Lower values suggest greater VH and higher values towards 1 suggest homogeneity.

A) relies on the nature of *single compartment* models used to estimate lung volume, where greater VH results in larger underestimation of lung volume[6]

B) relies on the IST estimation of lung volume (ELV) becoming more dependent on the period of the inspired sinewave with increasing VH[5,6]. So, ELV is estimated from two IST tests with different sinewave periods - 60 seconds (ELV_{60}) and 180 seconds (ELV_{180}).

Figure 2 The IST device

Methods

Study Design

52 patients with COPD and 48 healthy participants volunteered for the study (Table 1). COPD patients: FEV1/FVC ≤ 0.7, age ≥ 40 years, a smoking history (≥ 10 pack years). All participants underwent spirometry, body plethysmography and the transfer factor for carbon monoxide was measured.

This was followed by two IST tests: For 6 minutes participants breathed quietly through a face mask connected to a mainstream infrared N_2O and CO_2 sensor and an ultrasonic flow meter (fig 2). A mass flow controller added small quantities of N_2O to inspired gas – the concentration of which oscillates in a sinewave pattern at a period of either 60 sec or 180 sec.

Participant Characteristics

	COPD		Healthy	
N	52 (M/F = 30/22)		48 (M/F = 26/22)	
	Mean (SD)	% Pred	Mean (SD)	% Pred
Age (yrs)	66.5 (10.3)	-	53.5 (22)	-
Height (m)	1.7 (0.1)	-	1.7 (0.1)	-
Weight (kg)	79.4 (17.9)	-	71.5 (12)	-
BMI	27.7 (5.7)	-	24.9 (4.2)	-
FEV_1 (L)	1.6* (0.7)	56.2* (19.2)	3.3 (1)	102.4 (17.1)
FVC (L)	3.1* (1)	82.3* (21.8)	4.3 (1.3)	105.6 (18.5)
FEV_1%FVC	50.3* (14.8)	65.5* (17.6)	77.8 (6.9)	96.5 (7.5)
TLC (L)	6.8 (1.5)	112.3 (19.8)	6.3 (1.3)	105.4 (13.2)
RV (L)	3.5* (1.2)	152.4* (46.4)	2.2 (0.8)	104.4 (20.7)
FRC (L)	4.3* (1.3)	132.5* (38.1)	3.4 (0.8)	107.5 (16.6)
T_{LCO}	5.2* (1.8)	62.6* (19.1)	7.8 (2.6)	98.7 (15.5)
K_{CO}	1.1* (0.3)	76.6* (22.4)	1.5 (0.3)	94.6 (16)

Table 1, *Patient and healthy control participant characteristics. SD = standard deviation. M/F = Male/Female. * Significant difference from healthy control subject value (P<0.05).*

Results

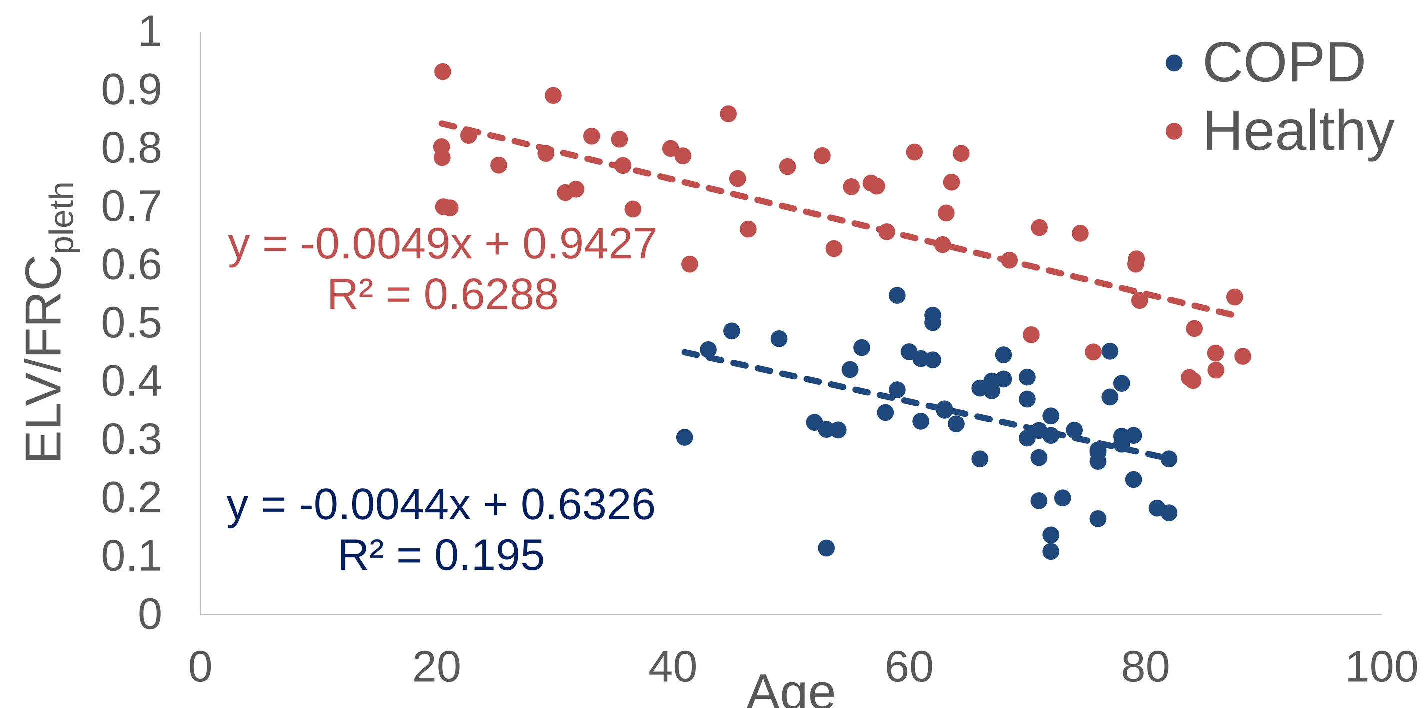

Figure 3 *ELV/FRC_{pleth} vs age for healthy participants and COPD patients*

Results

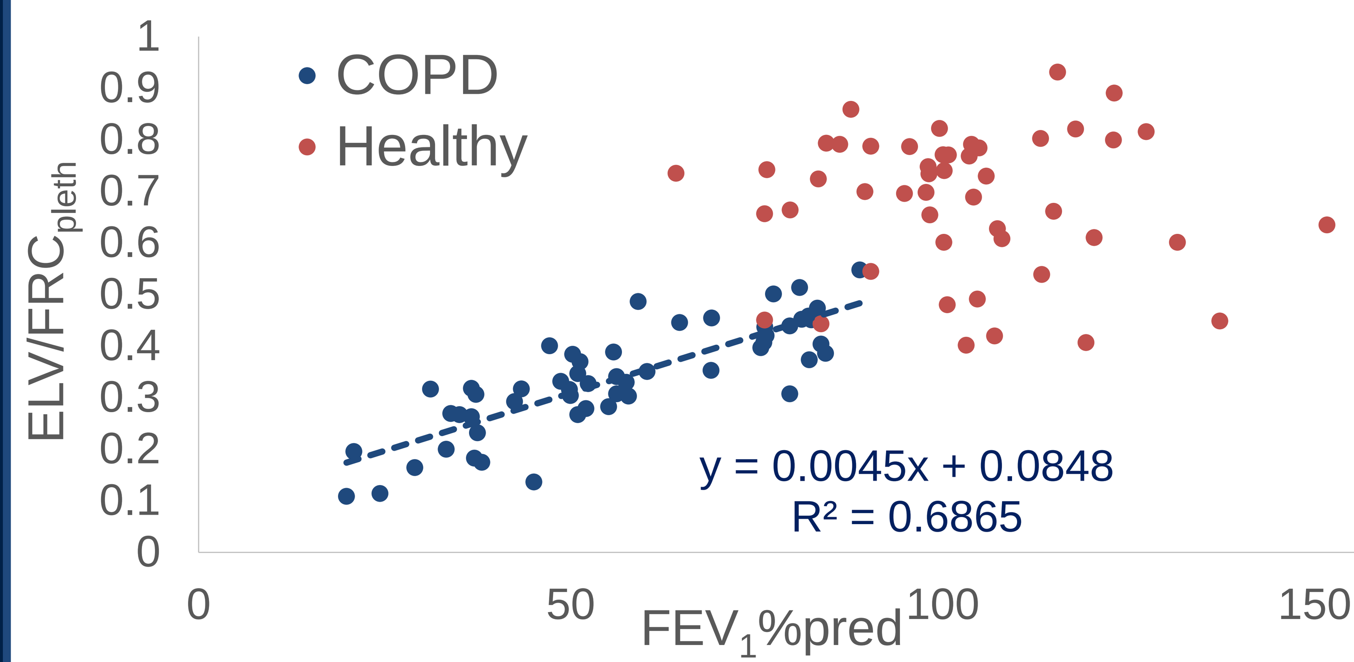

Figure 4: *ELV/FRC_{pleth} vs FEV_1 %pred for healthy participants and COPD patients*

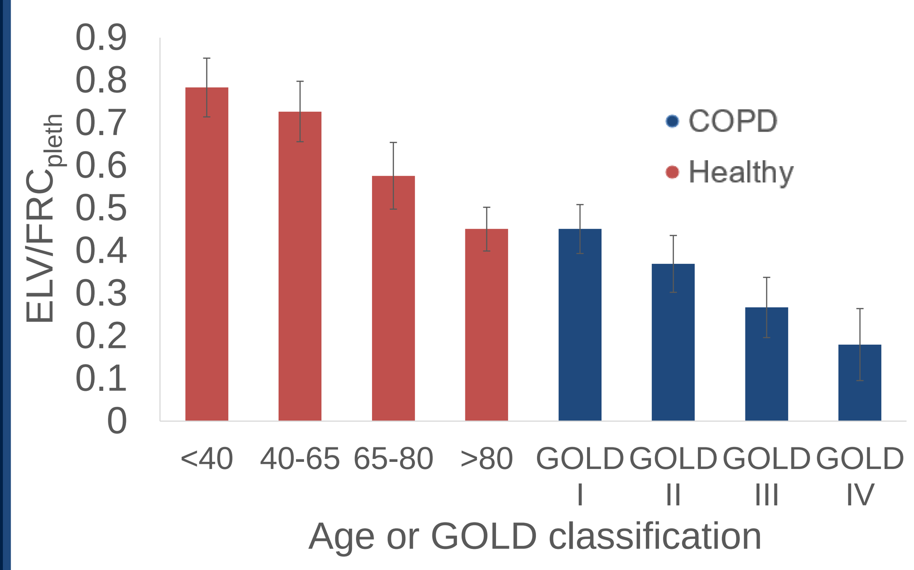

Figure 5: *Mean (± SD) ELV/FRC_{pleth} for different healthy age groups and GOLD classifications of airflow limitation in COPD.*

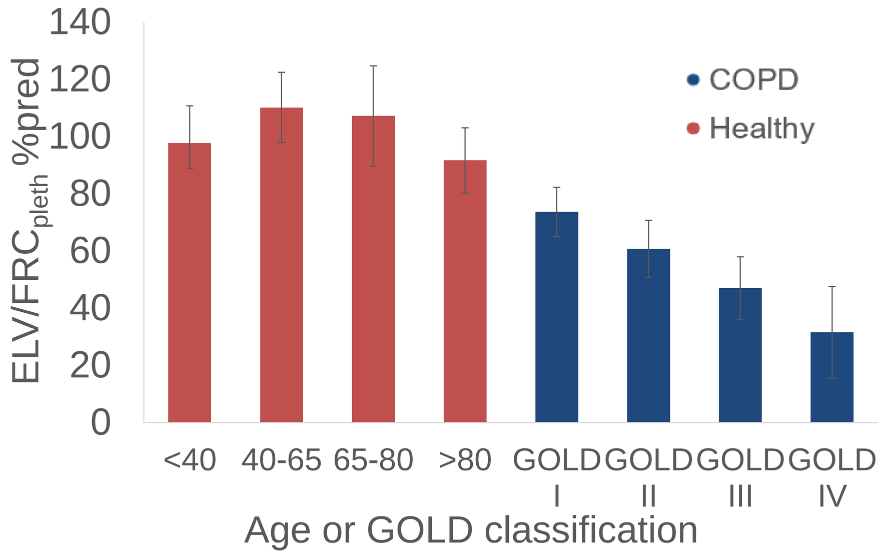

Figure 6: *Mean (± SD) ELV/FRC_{pleth} as a % predicted for age.*

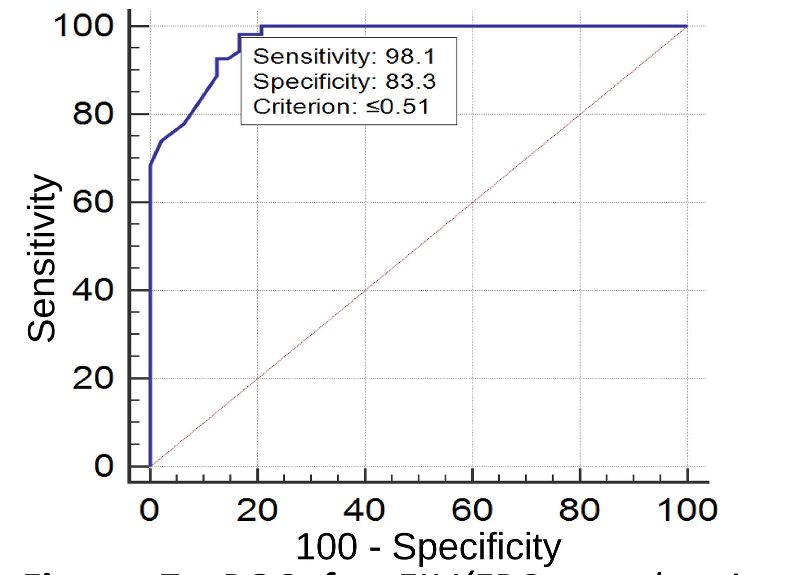

Figure 7: *ROC for ELV/FRC_{pleth}, showing diagnostic accuracy for COPD*

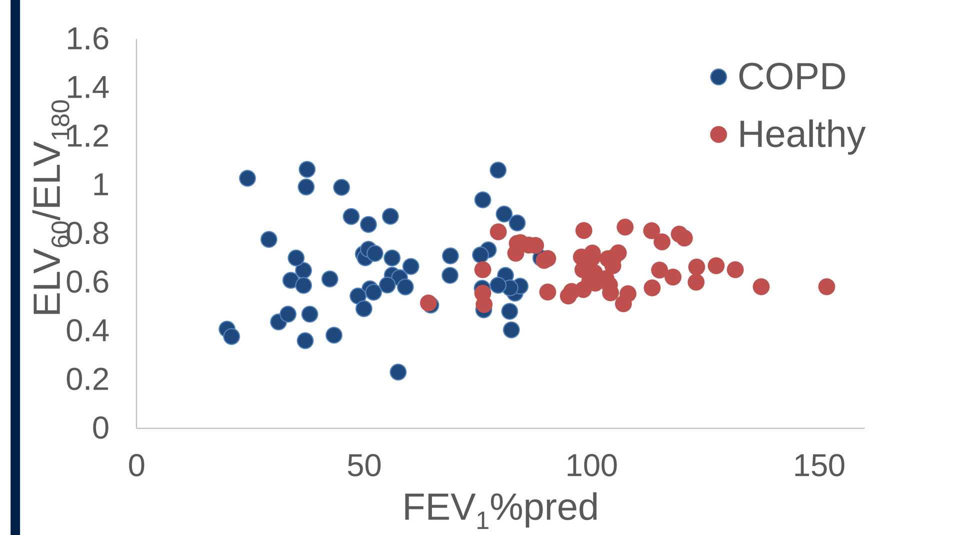

Figure 8: *ELV_{60}/ELV_{180} vs FEV_1 %pred for healthy participants and COPD patients*

Conclusions

There was a linear association between ELV/FRC_{pleth} and ageing in both health and COPD; and between ELV/FRC_{pleth} and the severity of airflow limitation (FEV_1 %pred) in COPD. No association was found with the ELV_{60}/ELV_{180} estimation of VH.

This suggests the IST estimate of VH (ELV/FRC_{pleth}) is sensitive to the decline in lung function associated with COPD. A cut off of ELV/FRC_{pleth} = 0.51, results in a very high true positive rate (sensitivity) and low false negative rate (100-specificity) for COPD (98.1, and 83.3 respectively). However normalising for the effects of healthy ageing on VH (ELV/FRC_{pleth} %pred) produces further specificity for COPD.

References:

1.Verbanck S, et al. Ventilation heterogeneity in the acinar and conductive zones of the normal ageing lung Thorax (2012)
2.Verbanck S, et al. Conductive and acinar lung-zone contributions to ventilation inhomogeneity in COPD. *Am J Resp Crit Care Med* 157.5 1573-1577. (1998).
3. Vogelmeier CF, et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease Report: GOLD. Eur Respir J. 2017;49(3) (2017)
4. Clifton L, et al. Assessment of lung function using a non-invasive oscillating gas-forcing technique', *Respir. Physiol. Neurobiol.*, vol. 189, no. 1, pp. 174–182 (2013)
5. Farmery A.D. Interrogation of the Cardiopulmonary System with Inspired Gas Tension Sinusoids. (2008)
6. Whiteley, et al. A tidal breathing model of the inert gas sinewave technique for inhomogeneous lungs. Respiration Physiology 124(1), 65–83. (2000)