Respiratory Medicine (2013) 107, 1700–1708

Available online at www.sciencedirect.com

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Reproducibility of arterial stiffness and wave reflections in chronic obstructive pulmonary disease: The contribution of lung hyperinflation and a comparison of techniques

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Received 12 February 2013; accepted 12 June 2013
Available online 3 August 2013

KEYWORDS
Vicorder;
SphygmoCor;
Pulse wave velocity;
Augmentation index;
COPD co-morbidities;
Cardiovascular disease

Summary
Significant cardiovascular morbidity and mortality exists in chronic obstructive pulmonary disease (COPD). Arterial stiffness is raised in COPD and may be a mechanistic link. Non-invasive assessment of arterial stiffness has the potential to be a surrogate outcome measure, although no reproducibility data exists in COPD patients.

Two studies (23 and 33 COPD patients) were undertaken to 1) assess the Vicorder reproducibility of carotid-femoral pulse wave velocity and Augmentation index in COPD; 2) compare it to SphygmoCor; and 3) assess the contribution of lung hyperinflation to measurement variability.

There were excellent correlations and good agreement between repeat Vicorder measurements for carotid-femoral pulse wave velocity ($r = 0.96$ ($p < 0.001$); mean difference $\pm$SD $= -0.03 \pm 0.36$ m/s ($p = 0.65$); co-efficient of reproducibility $= 4.02\%$; limits of agreement $= -0.68$–0.75 m/s). Augmentation index significantly correlated ($r = 0.736$ ($p < 0.001$); mean difference $\pm$SD $= 0.72 \pm 4.86\%$ ($p = 0.48$), however limits of agreement were only 10.42–9.02%, with co-efficient of reproducibility of 27.93%. Comparing devices,

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http://dx.doi.org/10.1016/j.rmed.2013.06.008

Vicorder values were lower but there was satisfactory agreement. There were no correlation between lung hyperinflation (as measured by residual volume percent predicted, total lung capacity percent predicted or the ratio of inspiratory capacity to residual volume) and variability of measurements in either study.

In COPD, measurement of carotid-femoral pulse wave velocity is highly reproducible, not affected by lung hyperinflation and suitable as a surrogate endpoint in research studies. Day-to-day variation in augmentation index highlights the importance of such studies prior to the planning and undertaking of clinical COPD research.

Introduction

Significant cardiovascular morbidity and mortality exists in chronic obstructive pulmonary disease (COPD) which is independent of shared risk factors such as smoking [1]. Different mechanisms linking these two common conditions have been proposed, including arterial stiffness, a surrogate shown to be an independent predictor of cardiovascular disease in a number of other chronic inflammatory conditions [2,3]. A spill over of inflammation from the pulmonary to the systemic circulation whose down-stream effects result in raised arterial stiffness could provide the mechanistic link between COPD and cardiovascular morbidity and mortality. Similarly neuro-humoral activation of the sympathetic nervous system as a result of lung hyperinflation may be a contributory factor [4].

Carotid-femoral pulse wave velocity (cfPWV) and Augmentation Index (AI) are non-invasive measures by which arterial stiffness can be measured. The arterial pressure wave is formed by a composite of ventricular contraction and a reflected wave that arrives back early in stiff arteries, adding to the forward wave, augmenting systolic pressure and forming the second systolic peak. This phenomenon can be quantified as the AI, defined as the difference between the 2 systolic peaks expressed as a percentage of the pulse pressure. It is derived from pulse wave analysis (PWA) where peripheral artery waveforms are acquired and validated transfer functions are used to derive values of the Aortic AI. cfPWV is estimated by measuring the transit time of the pulse wave between two pulse points [5].

A number of commercial devices exist for arterial stiffness measurement although at present no consensus exists as to which is the most accurate or reproducible. A novel relatively operator-independent device is now available which has potential advantages for screening programmes and use in intervention studies. It has compared favourably with the more established SphygmoCor device, considered by some to be the gold standard, in normal individuals, and those undergoing routine angiography [6,7]. Although CfPWV has been found to be raised in COPD and related to disease severity and other studies report on pulse wave analysis (PWA) [8,9], no data exist on the reproducibility of these devices in COPD patients, who due to their lung hyperinflation may have large intra-thoracic pressure swings with potentially significant breath-to-breath variation in the pulse wave. Such information is integral to the design and powering of longitudinal intervention studies.

The aim of this study was: 1) To assess the reproducibility of the Vicorder Device in measuring cfPWV and AI in COPD patients; 2) to compare the measurements with those of the SphygmoCor device in a second separate cohort of COPD patients and 3) furthermore assess the contribution of hyperinflation to the reproducibility of arterial stiffness measurements.

Materials and methods

Patients

Patients were prospectively enrolled from an existing COPD and cardiovascular disease database held at a university teaching hospital between October 2011 and August 2012. All patients were over 40 years of age, with a smoking history of at least 15 pack-years, and spirometric evidence of COPD according to ATS/ERS criteria. They were clinically stable with no history or recent exacerbations or long term oxygen therapy use. Demographic data and a full medical and therapeutic history were collected on all participants. Furthermore, lung function (spirometry and body plethysmograph) was performed in all participants. For the Vicorder reproducibility study (VRS) 23 consecutive patients had repeat measurements of cfPWV and PWA performed within 2 weeks of each other. For the Comparison study (VCS) with SphygmoCor a separate cohort of 33 consecutive COPD patients had cfPWV and PWA measurements performed on the same day with both devices. No patients in the VRS cohort were included in the VCS cohort. The study received a favourable review by the local research ethics committee and written informed consent was obtained from all patients.

Measurement techniques

Arterial stiffness

All measurements were performed by a single investigator with 18 months experience in arterial stiffness measurements (IS). IS was blinded to the previous results in the VRS but not the VCS since measures were collected on the same day for the latter study.

In the VCS the same brachial blood pressure was used to calibrate both devices. The SphygmoCor measurements were performed first, followed by the Vicorder measurements, in all cases.

All arterial stiffness measurements were in a temperature controlled room with the patient rested for 15 min in a