Cardiopulmonary Exercise Testing as a Longitudinal Clinical Tool in Interstitial Lung Disease Management

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**Rationale**: Interstitial lung disease (ILD) encompasses various fibrosing lung conditions including idiopathic pulmonary fibrosis (IPF) and hypersensitivity pneumonitis. Changes in forced vital capacity (FVC) and diffusion capacity for carbon monoxide ( $DL_{co}$ ) are the common clinical endpoints for prognostic monitoring and assessing treatment outcomes. Cardiopulmonary exercise testing (CPET) has become an important clinical measure for exercise capacity and prognosis in cardiac conditions; it provides assessment of the pulmonary, cardiovascular and skeletal muscle systems that cannot be evaluated by single organ system function. Therefore, its use in ILD remains largely unexplored. In this feasibility study, we investigated the use of CPET as a clinical measure in ILD and how the clinical variables change over time in a 30-week longitudinal study, to establish if commonly used variables such as FVC and  $DL_{co}$  change to the same extent as peak oxygen consumption ( $VO_{2peak}$ ) measured by CPET.

**Methods:** Thirteen patients with ILD undertook incremental exercise testing to exhaustion via electronically braked cycle ergometer. Variables included  $VO_{2peak}$ , FVC and  $DL_{co}$ . Pearson's correlation coefficients established relationships between variables. Patients were brought back 30 (± 10) weeks later for repeat testing to assess change over time. Paired samples t-tests established changes over time for each variable.

**Results:** At first visit, six of thirteen patients (46%) reached volitional exhaustion. Six CPETs were terminated early due to desaturation (SpO<sub>2</sub><88%) and one to exercise-induced right bundle branch block (recovery within minutes of ceasing exercise). Asymptomatic moderate exercise desaturation was common so we used less conservative SpO<sub>2</sub> termination criteria (SpO<sub>2</sub><82% or symptomatic desaturation) at subsequent visits. At second visit, eight of thirteen (62%) reached volitional exhaustion, four terminated due to symptomatic desaturation and one to poor ECG signal. The first visit showed a mean ( $\pm$  SD) FVC 83.9 $\pm$ 18.5%, DL<sub>CO</sub> 53.3 $\pm$ 9.3% and VO<sub>2peak</sub> 1.32 $\pm$ 0.35 Lmin<sup>-1</sup>. FVC and VO<sub>2peak</sub> were significantly correlated at baseline (r=0.80, p<0.05) whilst DL<sub>CO</sub> and VO<sub>2peak</sub> were not (r=32, p=0.31). Repeat testing showed a reduction in FVC to 82.9 $\pm$ 16.5% and DL<sub>cO</sub> to 50.5 $\pm$ 9.5%, but an increase in VO<sub>2peak</sub> to 1.37 $\pm$ 0.38 Lmin<sup>-1</sup>, however all changes were not significant (p>0.05). At the second visit, FVC and VO<sub>2peak</sub> were no longer significantly correlated (r=0.38, p>0.26) and the relationship between DL<sub>cO</sub> and VO<sub>2peak</sub> remained similar to baseline (r=0.33, p=0.36).

**Conclusions:** Preliminary CPET results in ILD have shown independent changes in FVC and  $VO_{2peak}$  over time. Further testing may therefore identify dynamic prognostic information that cannot be ascertained by static FVC and DL<sub>co</sub> measures alone.