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**Title:** Comparison of different measurement methods of gas diffusion in the lung

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**Body:** Background: Lung fibrosis results in decreases of oxygen diffusion and oxygen arterial partial pressure ( $P_{a,O_2}$ ) especially during exercise. Obstructive airway diseases are often associated with a mismatch of ventilation and perfusion. We investigated the validity of the CO diffusion capacity ( $D_{L,CO}$ ) in comparison with  $P_{a,O_2}$  and alveolo-arterial oxygen gradient ( $AaDO_2$ ) in different lung diseases. Methods: 250 subjects ( $52.3 \pm 12.5$  yrs) were examined, out of 206 there were: 13 with  $VC < LLN$  (normal  $FEV_1/VC$ ,  $D_{L,CO}$  normal or reduced); 19 with normal  $VC$  but  $D_{L,CO} < LLN$ ; 86 with mild or moderate bronchial obstruction ( $FEV_1/VC < LLN$ ,  $VC > LLN$ ), and 88 healthy controls. Pearson correlation coefficient of  $D_{L,CO}$  with  $P_{a,O_2}$  and  $AaDO_2$  were analyzed in each group. Results:  $D_{L,CO}$  (%pred.),  $P_{a,O_2}$  at rest, and  $AaDO_2$ , respectively, showed low correlation in all groups ( $0.25^{**}$ ;  $-0.19^*$ ) ( $**=p < 0.001$ ,  $*=p < 0.01$ ).  $D_{L,CO}$  and  $P_{a,O_2}$  during exercise revealed moderate correlation in the group with bronchial obstruction ( $0.55^{**}$ ), but there were strong correlations in the groups with reduced  $VC$  and/or  $D_{L,CO}$  ( $0.82^{**}$ ;  $0.68^*$ ). Correlations between  $D_{L,CO}$  and  $AaDO_2$  during exercise were the best in the latter two groups ( $-0.84^{**}$ ;  $-0.64^*$ ), medium in the group with bronchial obstruction ( $-0.47^{**}$ ), but not significant in healthy controls ( $0.19$ ). Conclusions: Only in patients with reduced  $VC$  and/or impaired  $D_{L,CO}$  all three parameters are likely to objectify impaired gas exchange in the lungs.  $AaDO_2$  relates to the ventilation, this may be the cause of the good correlation with  $D_{L,CO}$ . In the group with bronchial obstruction  $D_{L,CO}$  seems to be influenced by other pathophysiological aspects, resulting in only moderate correlation between the different parameters.