Supplemental Methods and Results

Cardiopulmonary Exercise Test Measurements:

Oxygen Uptake Efficiency Slope (OUES) was defined as the slope of VO_2 plotted against the semilog of total minute ventilation (VE). [1] % predicted peak VO2 was calculated using the Wasserman prediction equations.[2] VO_2/ work was calculated as the slope of the regression line between work (x-axis) and VO_2 (y-axis) starting 1-min in to incremental ramp exercise. VE was calculated as ventilation per minute (L/min) at the ventilatory anaerobic threshold (AT). [3] The ventilatory AT was measured by the V-slope method and was adjudicated by the study PI if values from two experienced readers differed by more than 5%. VO_2 was also collect at AT. The oxygen pulse slope was calculated by the slope of VO_2 versus heart rate. [3] For breathing reserve, maximum voluntary ventilation (MVV) was calculated as 35 x FEV1 as baseline. The equation 100 x (MVV – VE) / MVV, where VE was collected at either AT or peak exercise.

Pulmonary Function Test Measurements:

Participants with $FEV_1/FVC < 0.70$ and % predicted $FEV_1 \geq 80\%$ and $50\% \leq FEV_1 < 80\%$ were deemed to have obstructive lung disease classified as GOLD stage 1 and 2, respectively.[4,5] In addition, participants with $FEV_1/FVC < 0.7$ and % predicted $FVC < 80\%$ were defined as having restrictive lung physiology [6]

Computed Tomography Measurements:

CT images were acquired utilizing a 64-detector row scanner (Discovery, GE healthcare, Waukesha, WI, USA) with acquisition parameters of 120kVp, 300-350mA (based on body weight), 350ms rotation time, and 0.625mm section thickness. All scans were performed in the supine position, during inspiration, and without contrast. These CTs were visually assessed for radiographic changes using a modified sequential

reading method by three board-certified radiologists. [7] Emphysema was defined as present or absent based on visual inspection. [8] Interstitial lung abnormalities (ILA) were defined as non-dependent ground-glass, reticular abnormalities, diffuse centrilobular nodularity, nonemphysematous cysts, honeycombing or traction bronchiectasis that affected >5% of any lung zone. [9] Patchy, focal, or unilateral abnormalities were considered to be "indeterminate." [9]

Pulmonary Blood Vessel Measurements:

Vascular image analysis was performed in the Applied Chest Imaging Laboratory at Brigham and Women's Hospital using Chest Imaging Platform (www.chestimaging.platform.org). [10] Using an automated algorithm, three-dimensional reconstructions of the pulmonary vasculature were created using scale-space particles method.[10,11] As previously described, the vessel size at a certain location within the pulmonary system is determent by the particle scale information. [10,11]

Age interaction Results:

To further address the effect of age among non-smokers, we assessed age by quartile within the cohort through unadjusted scatter plots colored by age category (See Supplemental Figure 1) and linear models with an interaction between the age quartiles and pulmonary function (FEV_1, FVC, and DLCO). Based on inspection of the scatterplots, those in the older age quartiles have on average a lower peak VO2, but the effects of the pulmonary function variables on Peak VO_2 is constant across age quartiles (as seen from the parallel slopes in the scatterplots). This conclusion is further supported by the lack of significant p-values in the interaction models (See Supplemental Table 1; minimum p-value = 0.07). Our data does not provide evidence of differential effects of pulmonary function on peak VO_2 by age category.

In addition, we assessed age by quartile within the cohort through unadjusted scatter plots by age category (Supplemental Figure 2) and linear models with an interaction between the age quartiles and pulmonary blood vessel measurements (BV5 and TBV). Based on inspection of the scatterplots, those in the older age quartiles have on average a lower peak VO_2, but the effects of the blood vessel volume

variables on Peak VO_2 is constant across age quartiles. This conclusion is further supported by the lack of significant p-values in the interaction model (See Supplemental Table 1; minimum p-value = 0.6). Based on our data, age does not seem to modify the effects of blood vessel volume on peak VO_2.

References:

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