Supplemental Material

Data S1.

Supplemental Results

Exercise Hemodynamic Phenotyping by ΔmPAP/ΔCO slope

Semi-upright Rest and Exercise Hemodynamics

Healthy Control Cohort

The relationships between PA pressures and PAWP in controls are illustrated in Figure S1 Panel A-C. PA systolic pressure (PASP) and PA diastolic pressures (PADP) were linearly related to PAWP ($p<0.001$), with a minimal DPG. Healthy individuals presented on the vertical limb of the RpCp time relationship at rest, with a leftward shift with exercise. During exercise, there is a linear relationship between the decline in RpCp time and PAWP ($p<0.001$).

BREATH Cohort – ΔmPAP/ΔCO ≤3.2 WU

The relationship between PA pressures and PAWP in patients with ΔmPAP/ΔCO slope ≤3.2 WU are illustrated in Figure S1, Panel D-F. Similar to healthy controls, PASP and PADP were linearly related to PAWP during rest and exercise ($p<0.001$), with a minimal DPG. This group presented on the vertical limb of the RpCp time relationship during rest and exercise, with a linear relationship between the decline in RpCp time and PAWP ($p<0.001$).

BREATH Cohort – ΔmPAP/ΔCO >3.2 WU

The relationship between PA pressures and PAWP in patients with ΔmPAP/ΔCO slope ≥3.2 WU are illustrated in Figure S1, Panel G-I. In contrast to the other two groups, PASP was not related to PAWP. The linear relationship between PADP and PAWP was maintained ($p<0.001$), but DPG was elevated ($p=0.001$). This group presented on the horizontal limb of the

RpCp time relationship, but the relationship between the decline in RpCp time and PAWP was preserved ($p<0.001$).

Exercise Hemodynamic Phenotyping by Association of PAWP and Pulmonary Pressures: the PP/PAWP Ratio

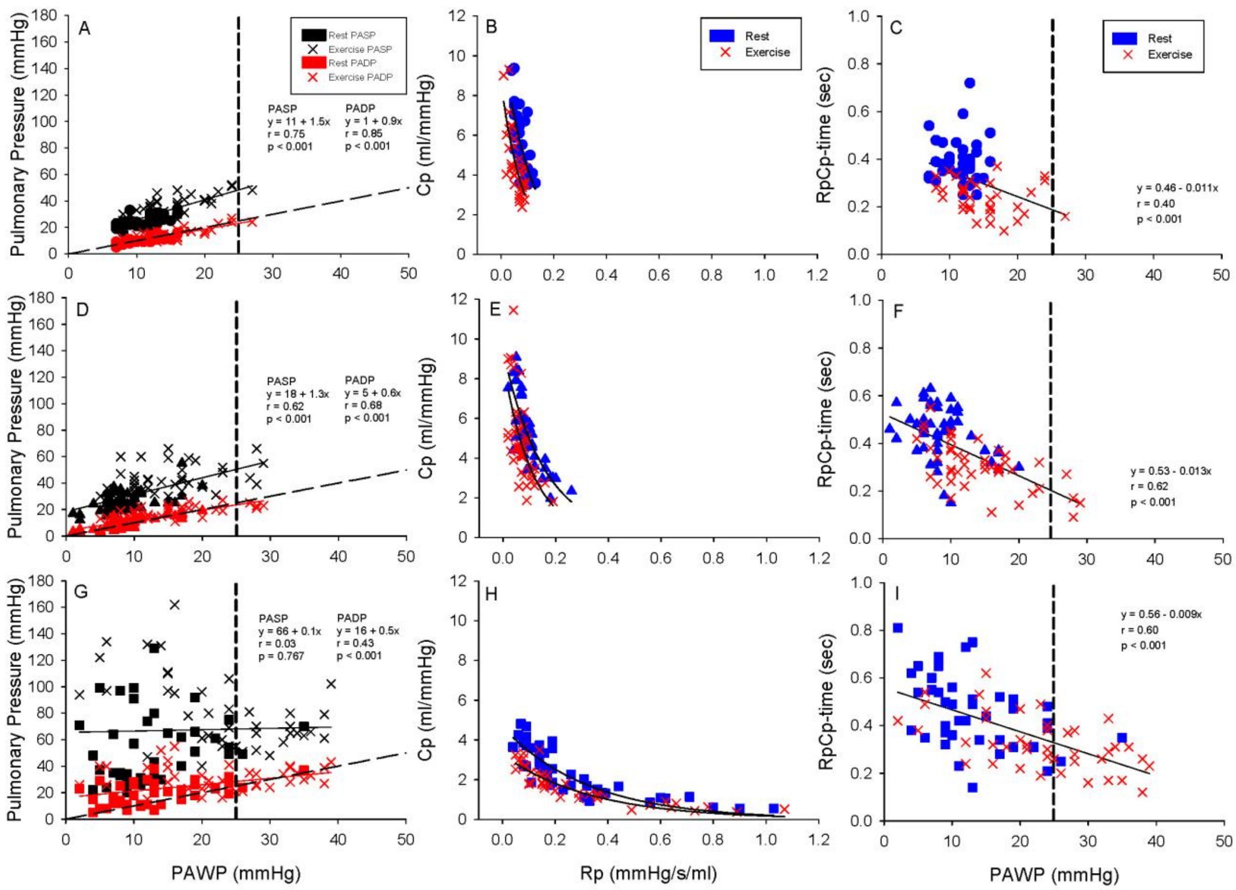
BREATH Cohort – ΔmPAP/ΔCO ≤3.2 WU

We then examined subgroups based on the PP/PAWP ≤ or > 2.5. The relationships between PA pressures and PAWP are illustrated in Figure S2. In both subgroups, linear relationships between PASP and PADP and PAWP were preserved (Panel A, D). However, in the exercise PP/PAWP >2.5 subgroup, the range of exercise PAWP responses was smaller and did not exceed 25 mmHg. Additionally, in this PP/PAWP >2.5 subgroup, both the increases in PASP and the declines in RpCp time were steeper for the same exercise increase in PAWP (Panel C, F).

BREATH Cohort – ΔmPAP/ΔCO >3.2 WU

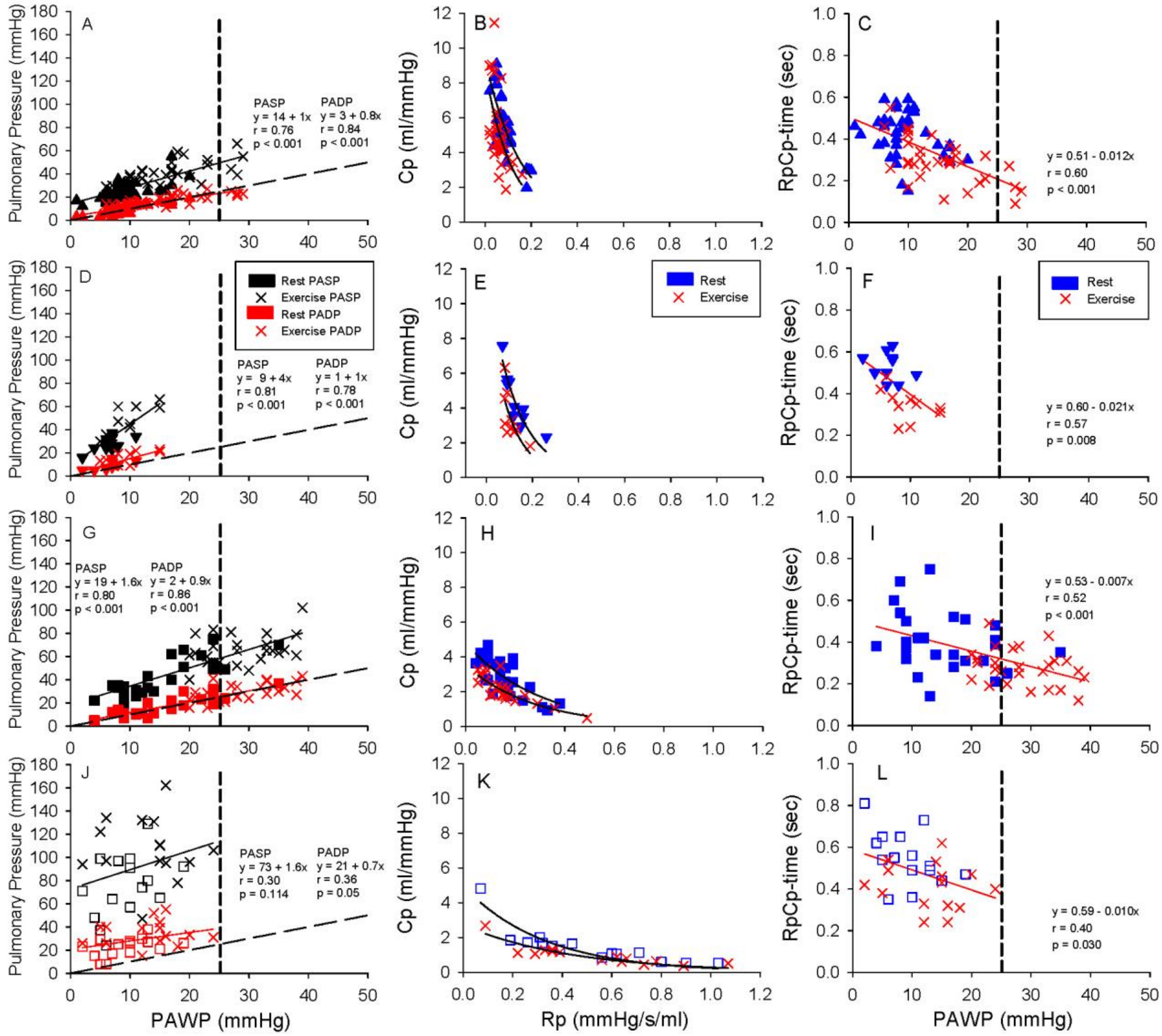
We again examined subgroups based on the PP/PAWP ≤ or > 2.5. The relationships between PASP and PADP and PAWP are illustrated in Supplemental Figure 2. In the exercise PP/PAWP ≤2.5 subgroup, the linear relationships between PAWP and PASP and PADP were preserved (all $p<0.001$) (Panel G). However, in the exercise PP/PAWP >2.5 subgroup, again there was a limited exercise PAWP responses that did not exceed 25 mmHg. This subgroup also demonstrated a larger DPG, and a loss of the linear relationship between PAWP and PASP (Panel J). Both the PP/PAWP subgroups continued to demonstrate linear relationships between PAWP and the decline in RpCp time (Panel I, L).

Figure S1. Pulmonary hemodynamics at semi-upright rest and during steady state submaximal exercise.



Panel A-C: Healthy control cohort. *Panel D-F:* BREATH cohort ΔmPAP/ΔCO ≤3.2 WU. *Panel G-I:* BREATH cohort ΔmPAP/ΔCO >3.2 WU. Linear regression regressions are denoted within each panel. Vertical dashed line represents end-expiratory pulmonary artery wedge pressure of 25 mmHg. *Panel A, D, G* diastolic pressure gradient of 1 mmHg is plotted.

Figure S2. Pulmonary hemodynamics at semi-upright rest and during steady state submaximal exercise.



Panel A-C: BREATH cohort ΔmPAP/ΔCO ≤3.2 WU, Exercise PP/PAWP ≤2.5. *Panel D-F:* BREATH cohort ΔmPAP/ΔCO ≤3.2 WU, Exercise PP/PAWP >2.5. *Panel G-I:* BREATH cohort ΔmPAP/ΔCO >3.2 WU, Exercise PP/PAWP ≤2.5. *Panel J-L:* BREATH cohort ΔmPAP/ΔCO >3.2 WU, Exercise PP/PAWP >2.5. Linear regression regressions are denoted within each panel. Vertical dashed line represents end-expiratory pulmonary artery wedge pressure of 25 mmHg. *Panel A, D, G, J* diastolic pressure gradient of 1 mmHg is plotted.