Respiratory muscle work and oxidative stress in the elderly: impact on blood flow and fatigue.

SPECIFIC AIMS

Compared to young individuals, older subjects are characterized by substantially increased respiratory muscle work ($W_r$), and elevated oxidative stress - especially during exercise (14, 18, 22). Considering these observations, two specific findings in young healthy humans form the rationale for this proposed project: First, relieving much of $W_r$ during cycling exercise via ventilatory assist increases leg blood flow ($Q_{leg}$) and $O_2$ delivery (11, 12). Second, end-exercise locomotor muscle fatigue is significantly ameliorated by relieving much of $W_r$ (1, 7) and oxidative stress (16) normally incurred during sustained endurance exercise.

Based on these findings, we propose the following specific aims:

1. What is the impact of $W_r$ and oxidative stress on muscle fatigue and exercise tolerance in the elderly?
   a) Determine the effects of constant-load cycling exercise-induced $W_r$ on locomotor muscle fatigue, systemic oxidative stress, and exercise tolerance.
      \textit{Hypothesis:} Relieving much of the exercise-induced $W_r$ via pressure support ventilation will significantly reduce the development of quadriceps fatigue and attenuate systemic oxidative stress resulting in a significantly greater improvement in endurance time to exhaustion in the elderly compared to young individuals.
   b) Determine the effects of cycling exercise-induced systemic oxidative stress on locomotor muscle fatigue and exercise tolerance.
      \textit{Hypothesis:} Attenuating exercise-induced oxidative stress via intravenous antioxidant infusion will reduce the development of quadriceps fatigue and improve endurance time to exhaustion significantly more in the elderly compared to young individuals.

2. Is the age-related impact of $W_r$ and oxidative stress on locomotor muscle fatigue mediated by $Q_{leg}$?
   a) Determine the impact of exercise-induced $W_r$ on $Q_{leg}$ and the associated impact on locomotor muscle oxidative stress generation.
      \textit{Hypothesis:} Relieving much of the exercise-induced $W_r$ via pressure support ventilation plus heliox will increase $Q_{leg}$ and attenuate locomotor muscle oxidative stress generation significantly more in the elderly compared to young individuals.
   b) Determine the impact of exercise-induced systemic oxidative stress on $Q_{leg}$.
      \textit{Hypothesis:} Attenuating exercise-induced oxidative stress via intravenous antioxidant infusion will increase $Q_{leg}$ significantly more in the elderly compared to young individuals.

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