



# Expiratory flow limitation and operating lung volumes during exercise in older and younger adults

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## ABSTRACT

We determined the effect of aging on expiratory flow limitation (EFL) and operating lung volumes when matched for lung size. We hypothesized that older adults will exhibit greater EFL and increases in EELV during exercise compared to younger controls. Ten older (5 M/5W; >60 years old) and nineteen height-matched young adults (10 M/9W) were recruited. Young adults were matched for %predicted forced vital capacity (FVC) (Y-matched %Pred FVC; n = 10) and absolute FVC (Y-matched FVC; n = 10). Tidal flow-volume loops were recorded during the incremental exercise test with maximal flow-volume loops measured pre- and post-exercise. Compared to younger controls, older adults exhibited more EFL at ventilations of 26, 35, 51, and 80L/min. The older group had higher end-inspiratory lung volume compared to Y-matched %Pred FVC group during submaximal ventilations. The older group increased EELV during exercise, while EELV stayed below resting in the Y-matched %Pred FVC group. These data suggest older adults exhibit more EFL and increase EELV earlier during exercise compared to younger adults.

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## 1. Introduction

During heavy exercise, expiratory flow limitation (EFL) is prevalent in endurance-trained men (Johnson et al., 1992; Guenette et al., 2007) and women (McClaran et al., 1998; Guenette et al., 2007), aging (Johnson et al., 1991a,b) and to a lesser extent recreationally-active men and women (Smith et al., 2014; Chenoweth et al., 2015). EFL has previously been shown to limit ventilation (McClaran et al., 1998; McClaran et al., 1999), increase dyspneic sensations (Iandelli et al., 2002; Chenoweth et al., 2015) and work of breathing, and is associated with a tendency for EELV to increase towards resting values during heavy exercise (Pellegriano et al., 1993). In fact, increasing the capacity of the pulmonary system (i.e. maximum flow-volume loop) has been shown to reduce EFL (McClaran et al., 1998; McClaran et al., 1999; Smith et al., 2014; Chenoweth et al., 2015), lessen dyspneic sensations during exercise (Chenoweth et al., 2015) and improve exercise performance (Wilkie et al., 2015).

In contrast, aging leads to changes within the pulmonary system that ultimately leads to a reduced maximum flow-volume loop. Specifically, aging is associated with the loss of elastic recoil (Knudson et al., 1977), stiffening of the chest wall (Johnson et al.,

1994), and decreased respiratory muscle strength (Harik-Khan et al., 1998). Over twenty years ago, it was suggested that older adults have greater severity of EFL for a given ventilation during exercise (Johnson et al., 1994; McClaran et al., 1995); however, the subjects were not matched for pulmonary function limiting the interpretation of these results. Previous studies have specifically investigated the influence of aging on the development of EFL during exercise (Johnson et al., 1994, 1991a,b; Ofir et al., 2008; Faisal et al., 2015; Wilkie et al., 2012; DeLorey and Babb, 1999). However, these previous studies have only reported the severity of EFL at the respiratory compensation point and/or  $\dot{V} O_{2peak}$  (Wilkie et al., 2012; Faisal et al., 2015; DeLorey and Babb, 1999), only tested women (Wilkie et al., 2012), or did not have a younger control group (Johnson et al., 1991a,b). In addition, discrepancy exists in the literature as to whether end-expiratory lung volume (EELV) decreases at the onset of exercise in older adults (DeLorey and Babb, 1999; Johnson et al., 1991a) and if they display an earlier and/or greater increase in EELV during exercise compared to younger adults (DeLorey and Babb, 2000; Faisal et al., 2015; Wilkie et al., 2012). To address these issues, we compared the severity of EFL and operating lung volumes at submaximal and peak ventilations during an incremental test with height-matched older and younger adults matched for % predicted lung size. In addition, we examined how the age-induced changes in expiratory flow rates affected the severity of EFL and operating lung volumes by matching absolute lung size. Therefore, our primary purpose of this study

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was to determine the development of EFL and operating lung volumes during exercise in older and younger adults matched for a) % predicted lung volume as previously done (Wilkie et al., 2012) and b) absolute lung volume. We hypothesized that the older adults would have greater severity of EFL as well as greater increases in EELV compared to height-matched younger adults during exercise.

## 2. Methods

Ten older adults (5 men, 5 post-menopausal women) and nineteen younger adults (10 men, 9 pre-menopausal women) were recruited to participate in this study. For the current study, two younger control groups were used. Young adults were matched with older adults for %predicted forced vital capacity (FVC) (Y-matched%Pred FVC) using established predicted equations (Knudson et al., 1983) and absolute FVC (Y-matched FVC). These groups were also sex- and height-matched. One pre-menopausal woman was in both Y-matched%Pred FVC and Y-matched FVC groups. Subjects were recruited with a range of physical activity levels, reported no history of smoking within the past 10 years, no history of asthma or any other respiratory condition and healthy as determined by self-report from a medical health questionnaire. Exclusion criteria included existence of acute and/or chronic cardiovascular, pulmonary or metabolic diseases. Pre-menopausal women were tested randomly throughout their menstrual cycle as female sex hormones do not influence exercising ventilation (Smith et al., 2015; Beidleman et al., 1999; Macnutt et al., 2012) or chemosensitivity (Macnutt et al., 2012). Informed consent was obtained prior to participation in the study which was approved by Institutional Review Board of Human Subjects at Kansas State University, Manhattan, KS and conformed to the Declaration of Helsinki.

### 2.1. Study design

For this cross-sectional study, all exercise testing was performed on one visit in the laboratory. First, subjects were familiarized with experimental procedures and equipment. Next, subjects performed an incremental cycling test to exhaustion to determine peak aerobic capacity ( $\dot{V} O_{2peak}$ ). During the incremental test, subjects performed inspiratory capacity (IC) maneuvers for measurement of EELV and EFL. Subjects completed pulmonary function tests (PFTs) prior to and following the incremental test.

### 2.2. Peak aerobic capacity ( $\dot{V} O_{2peak}$ )

An incremental exercise test on an electromagnetic cycle ergometer (800S, Sensor Medics Corp., Yorba Linda, CA) to exhaustion was performed to determine  $\dot{V} O_{2peak}$ . Baseline metabolic and ventilatory measurements were collected (SensorMedics 229 Metabolic Cart, SensorMedics Corp., Yorba Linda, CA, USA) for three minutes. Subjects were then instructed to remain seated throughout the test and maintain 60–80 revolutions per min (rpm). Subjects performed a three min warm-up at 20 W and then the workload increased 25 W every min until volitional exhaustion despite continual verbal encouragement. The incremental exercise test was terminated when subjects could not maintain the pedal frequency >60 rpm for five consecutive revolutions. Metabolic and ventilatory data were continuously monitored breath-by-breath throughout exercise and averaged over 20 s. Heart rate (HR) was collected continuously and was recorded at the end of each stage.

### 2.3. Pulmonary function tests

Pulmonary function tests were assessed according to American Thoracic Society/European Respiratory Society guidelines (Miller

et al., 2005). Prior to data collection, multiple practice sessions were conducted until valid, consistent measurements were obtained. Maximum flow-volume loops (MFVL) were assessed prior to and following the  $\dot{V} O_{2peak}$  test (SensorMedics 229 Metabolic Cart, SensorMedics Corp., Yorba Linda, CA, USA). The MFVL gave measures of forced expiratory volume in one second ( $FEV_1$ ), forced vital capacity (FVC), forced expiratory flow at 50% ( $FEF_{50}$ ) and between 25 and 75% ( $FEF_{25-75}$ ) of FVC, and peak expiratory flow rate (PEF).

### 2.4. Determination of EFL and tidal volume

During exercise, EFL was assessed by recording tidal volume ( $V_T$ ) loops using a bidirectional flow sensor with the gas analyzer. The system's software allows for quality control checks (both during and after the test) to ensure proper (and consistent) IC maneuvers. Three to four MFVL maneuvers were performed by each subject before and immediately following exercise with the largest loop (post-exercise) used for analysis. An IC maneuver was performed from functional residual capacity to determine placement of  $V_T$  during the last 20 s of each min during the  $\dot{V} O_{2peak}$  test. The severity of EFL was measured as the intersection of the tidal volume loop with the MFVL divided by the tidal volume (Johnson et al., 1999; Smith et al., 2014; Chenoweth et al., 2015). Assuming total lung capacity did not change significantly during exercise (Johnson et al., 1991a,b), EELV was determined by subtracting the IC volume from the FVC (Johnson et al., 1999). A "typical" breath was determined if it had similar volume and flow characteristics to the previous breaths before the IC maneuver. The metabolic cart automatically corrects for drift that occurs when there are differences between inspiratory and expiratory volumes. EFL was determined as present when the exercising  $V_T$  intersected the MFVL by  $\geq 5\%$  (Chapman et al., 1998).

### 2.5. Statistical analysis

Data are reported as mean  $\pm$  SD. Differences in subject characteristics, resting pulmonary function, and  $\dot{V} O_{2peak}$  data between older adults and younger controls (Y-matched%Pred FVC and Y-matched FVC) were determined by unpaired *t*-tests. A two-way mixed factorial measures analysis of variance (ANOVA) (group  $\times$  ventilation (i.e. 10, 20, 26, 35, 51 and 80 L/min)) was used to compare operating lung volumes (EELV and end-inspiratory lung volume (EILV)), %EFL, and ventilatory variables (ventilation ( $\dot{V}_E$ ), tidal volume ( $V_T$ ), breathing frequency ( $F_b$ ),  $V_T$ /FVC, and ventilatory equivalent carbon dioxide ( $\dot{V}_E/VCO_2$ )). A Tukey's post hoc analysis was performed to determine where significant differences existed. Significance was set at  $p < 0.05$ .

## 3. Results

### 3.1. Subject characteristics

Subject characteristics and resting pulmonary function are shown in Table 1 and peak metabolic and ventilatory data are displayed in Table 2. The older and Y-matched%Pred FVC groups were matched for height ( $p = 0.97$ ) and %predicted PEF ( $p = 0.59$ ), FVC ( $p = 0.89$ ),  $FEV_1$  ( $p = 0.63$ ),  $FEF_{25-75}$  ( $p = 0.12$ ), and  $FEF_{50}$  ( $p = 0.99$ ). The older group had significantly lower FVC ( $p = 0.03$ ),  $FEV_1$  ( $p < 0.01$ ),  $FEF_{25-75}$  ( $p < 0.01$ ), and  $FEF_{50}$  ( $p = 0.05$ ), but not different PEF ( $p = 0.09$ ) compared to Y-matched%Pred FVC. At peak exercise, the older group had lower absolute  $\dot{V} O_2$  ( $p < 0.01$ ), relative  $\dot{V} O_2$  ( $p < 0.01$ ),  $\dot{V} CO_2$  ( $p < 0.01$ ),  $\dot{V}_E$  ( $p = 0.02$ ),  $F_b$  ( $p < 0.01$ ), HR ( $p < 0.01$ ) and power ( $p = 0.03$ ), while  $V_E/VO_2$  ( $p = 0.15$ ) and  $PetCO_2$  ( $p = 0.39$ ) were not different compared to the Y-matched%Pred FVC.

The older and Y-matched FVC groups were matched for height ( $p = 0.76$ ) and FVC ( $p = 0.42$ ). The older group had lower  $FEV_1$

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