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Exercise-related change in airway blood flow in humans: Relationship to changes in cardiac output and ventilation

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Abstract

This study examined the relationship between airway blood flow (\dot{Q}_{aw}), ventilation (\dot{V}_E) and cardiac output (\dot{Q}_{tot}) during exercise in healthy humans ($n = 12$, mean age 34 ± 11 yr). \dot{Q}_{aw} was estimated from the uptake of the soluble gas dimethyl ether while \dot{V}_E and \dot{Q}_{tot} were measured using open circuit spirometry. Measurements were made prior to and during exercise at 34 ± 5 W (Load 1) and 68 ± 10 W (Load 2) and following the cessation of exercise (recovery). \dot{Q}_{aw} increased in a stepwise fashion ($P < 0.05$) from rest ($52.8 \pm 19.5 \mu\text{l min}^{-1} \text{ml}^{-1}$) to exercise at Load 1 ($67.0 \pm 20.3 \mu\text{l min}^{-1} \text{ml}^{-1}$) and Load 2 ($84.0 \pm 22.9 \mu\text{l min}^{-1} \text{ml}^{-1}$) before returning to pre-exercise levels in recovery ($51.7 \pm 13.2 \mu\text{l min}^{-1} \text{ml}^{-1}$). \dot{Q}_{aw} was positively correlated with both \dot{Q}_{tot} ($r = 0.58$, $P < 0.01$) and \dot{V}_E ($r = 0.50$, $P < 0.01$). These results demonstrate that the increase in \dot{Q}_{aw} is linked to an exercise related increase in both \dot{Q}_{tot} and \dot{V}_E and may be necessary to prevent excessive airway cooling and drying.

Keywords

Bronchial blood flow; Cardiac output; Ventilation

1. Introduction

During exercise there is a dynamic increase in the dimensions of the conducting airways resulting in a decrease in the resistance to airflow and an increase in alveolar ventilation (de Bisschop et al., 2003). While these dynamic changes in airway dimensions are well characterized, changes in the blood flow to the conducting airways themselves (i.e., airway blood flow, \dot{Q}_{aw}) are not so well defined.

In humans, the majority of the blood flow to the conducting airways is via the bronchial artery with the remaining flow arising from bronchopulmonary anastomoses (Deffebach et al., 1987). Airway blood flow represents only about 1% of the total pulmonary blood flow (\dot{Q}_{tot}) (Coleridge and Coleridge, 1994), however changes in \dot{Q}_{aw} may be important during exercise to maintain airway function by preventing excessive airway cooling and drying (Parsons et al., 1989). For example, in humans, Kim et al. (1996) demonstrated that \dot{Q}_{aw} increased during

eucapnic hyperventilation (\dot{V}_E) with frigid air. Similarly there is evidence that \dot{Q}_{aw} increases during eucapnic hyperventilation in sheep (Parsons et al., 1989).

To date, the results of studies that have examined changes in \dot{Q}_{aw} during exercise in animals remain controversial. Two studies by Manohar and coworkers (Manohar, 1990; Manohar et al., 1992) have reported that \dot{Q}_{aw} , measured using microspheres, increased during exercise in ponies. In contrast, Bishop et al. (2007) reported that \dot{Q}_{aw} , measured using a flowmeter mounted on the bronchial artery, decreased during incremental exercise in sheep.

While these differential responses in \dot{Q}_{aw} during exercise may be species specific (Coleridge and Coleridge, 1994), to date no study has examined changes in \dot{Q}_{aw} during exercise in humans. One reason for the failure to examine these changes during exercise in humans is the invasive nature of the techniques required to measure \dot{Q}_{aw} . The development of the non-invasive method using the soluble gas dimethyl ether (DME) has made the measurement of \dot{Q}_{aw} far more practical in humans (Wanner et al., 1988). This technique, which has been validated against accepted invasive techniques in animals (Scuri et al., 1995), is relatively easy to use and can be performed during low to moderate-intensity, steady-state exercise in humans.

Therefore, the aim of this study was to measure \dot{Q}_{aw} in healthy untrained subjects at different levels of exercise intensity and to determine the relationship between changes in \dot{Q}_{aw} , \dot{Q}_{tot} and \dot{V}_E . We hypothesized that a progressive rise in \dot{Q}_{aw} would occur as exercise intensity was increased. Moreover, we hypothesized that the rise in \dot{Q}_{aw} , with a stepwise increase in submaximal exercise intensity, would be associated with a corresponding rise in \dot{Q}_{tot} and \dot{V}_E .

2. Methods

2.1. subject details and exercise protocol

Twelve healthy subjects (7 females and 5 males) participated in this study. subject details are provided in Table 1. Spirometry results indicate that subjects were free of lung disease. subjects were also normotensive and not taking any prescription medications for control of blood pressure or bronchial asthma. The Mayo Clinic Institutional review board approved the study and all subjects signed a written consent form prior to commencement.

\dot{Q}_{aw} and \dot{Q}_{tot} were measured pre-exercise, at each of two different exercise Loads (exercise Load 1 and Load 2) and post-exercise. For male subjects, exercise Load 1 and Load 2 typically corresponded to cycling on a stationary ergometer (Corival 400, St. Paul, MN, USA) at 40 and 80 W, respectively. The two exercise loads for female subjects typically corresponded to cycling at 30 and 60 W respectively. Exercise loads were determined following pilot testing and familiarization to determine each subject's ability to perform breath-holding required for measuring \dot{Q}_{aw} .

Subjects exercised for 10 min at each of the corresponding workloads. Dual measures of \dot{Q}_{tot} were made at 3 and 5 min of exercise, while the measurement of \dot{Q}_{aw} was obtained between minutes 6 and 10 of exercise. Recovery measures of \dot{Q}_{tot} were made 3 and 5 min post exercise, while the recovery measurement of \dot{Q}_{aw} was obtained between minutes 6 and 10 after the cessation of exercise.

Systolic and diastolic blood pressure measurements were made using auscultation prior to and during each of the exercise loads and during the recovery period. Mean arterial pressure was calculated by summing the diastolic blood pressure and one third of the pulse pressure.

2.2. Determination of airway blood flow

Airway blood flow was determined using the modified soluble, gas DME technique that has previously been described (Scuri et al., 1995; Wanner et al., 2006). DME has a high solubility in tissue and blood (Bunsen solubility coefficient of DME, α , in tissue and blood is 9 ml ml⁻¹ at 37° C). When inhaled into the pulmonary dead space (V_D) DME has a biphasic pattern of uptake following equilibration. The first rapid phase of uptake will occur when DME dissolves in the tissue. The slower second phase of uptake occurs as the blood flow in the bronchial capillaries take up DME. Assuming rapid equilibration of DME within the airways and tissue, then the steady-state uptake of the DME (\dot{V}_{DME}) over a defined segment of the conducting airway will be proportional with \dot{Q}_{aw} (Scuri et al., 1995). Airway blood flow can be calculated using mass balance as:

$$\dot{Q}_{aw} = \frac{\dot{V}_{DME}}{\alpha F_{DME}}$$

where F_{DME} represents the mean fractional concentration of DME and α the solubility coefficient of DME in blood. \dot{V}_{DME} can be calculated from the slope of the mean expired DME concentration over time multiplied by the volume of the defined airway segment in the conducting airways (V_S). The DME concentration was determined from phase 1 of the expired nitrogen (N_2) washin curve. In the current study, the defined airway segment (V_S) was determined as:

$$V_S = V_{D,min} - 20 \text{ ml.}$$

where $V_{D,min}$ is the minimal dead space volume, determined from the volume exhaled to the point of initial departure of exhaled F_{N_2} from room air. Twenty milliliters represent the first 20 ml exhaled at the end of breath-hold and represents the oropharyngeal volume.

In the equation, α is defined as the volume of gas at standard, temperature and pressure dry (STPD) dissolved in 1 ml of liquid at 760 mmHg measured at body temperature (37° C or 310 K) where the water vapour pressure is 47 mmHg. All other elements in the equation are corrected accordingly. V_S was measured under body temperature pressure saturated (BTPS) conditions. When corrected, the STPD factor for V_S is $[(760 - 47) \times 273] / [760 \times 310]$ or 0.83.

Hence $\dot{Q}_{aw} = 0.83(V_{D,min} - 20 \text{ ml}) \times (\text{slope of mean expired DME concentration}) / (\alpha F_{DME})$.

Normalising the measurement of \dot{Q}_{aw} to the dead space volume from which DME uptake is measured (i.e., $V_{D,min} - 20 \text{ ml}$), this equation reduces to:

$$\dot{Q}_{aw} = \frac{0.83 \times (\text{slope of mean expired DME concentration})}{\alpha F_{DME}}$$

where \dot{Q}_{aw} is expressed in microliters per minute per milliliter of dead space.

2.3. Technique for measurement of airway blood flow

See Fig. 1 for a schematic representation of the experimental setup. To measure \dot{Q}_{aw} , the subject breathed through a mouthpiece connected in series to a heated pneumotachometer (Custom Series 3700, Hans Rudolph, Kansas City, MO, USA), a shutter valve (Series 4260A, Hans Rudolph, Kansas City, MO, USA) and a 3-way slide valve (Series 8560A, Hans Rudolph, Kansas City, MO, USA). The 3-way slide valve was connected to a reservoir tank containing

9% DME in a balance of N₂. The total dead space in this system was less than 44 ml. Concentrations of DME and N₂ were sampled at the mouth using a mass spectrometer (MGA 1100, Perkins Elma, MA Tech, St Louis, MO, USA). The signals from the pneumotachometer and the mass spectrometer were time aligned and sent to a computer via an analogue-to-digital board (Measurement Computing, PCI DAS 6034, Norton, MA, USA) where they were processed using custom written software.

To measure \dot{Q}_{aw} , subjects performed a four-step maneuver (Fig. 1). In the first step, the subject breathed out 500 ml (Fig. 1a) from total lung capacity (TLC). In the second step, the slide valve port to the reservoir tank containing DME and N₂ was opened and the subject rapidly inhaled back up to TLC (Fig. 1b) via a demand valve (01DV2000, O-Two Medical Technologies, Mississauga, CA, USA). In the third step, the subject breath-held for a pre-determined period during which time the shutter valve was closed (Fig. 1c). In the fourth step, the subject breathed out through a flow resistor designed to standardize expiratory flow (Fig. 1d).

For each measurement of \dot{Q}_{aw} , each subject performed maneuvers with two sets of breath-hold times of 5, 8 and 10s. In our laboratory, the test-retest reliability for determining \dot{Q}_{aw} is 0.98 in 8 healthy subjects (mean age 31 ± 9 yr) with a coefficient of variation of 3.8%.

2.4. Measurement of oxygen uptake

Oxygen uptake ($\dot{V}O_2$), \dot{V}_E and end-tidal CO₂ ($P_{ET}CO_2$) were measured breath-by-breath using a metabolic measuring system (CPX-D, Medical Graphics Corporation, St. Paul, MN, USA). In the present study $P_{ET}CO_2$ was measured to provide a non-invasive estimate of P_aCO_2 (Weinger and Brimm, 1987). Metabolic data were collected for a 3-min period at rest, during each of the exercise loads and during recovery.

2.5. Measurement of cardiac output

\dot{Q}_{tot} was measured using the open-circuit acetylene washin technique. This technique has been validated using the direct Fick method in healthy adults and is not influenced by breathing pattern and does not create further breathlessness by a build up of CO₂ (no rebreathing, Johnson et al., 2000). The average of the two repeated measures was reported as the \dot{Q}_{tot} .

2.6. Calculation of bronchial vascular resistance

Bronchial vascular resistance (BVR) was determined from the ratio of bronchial perfusion pressure and \dot{Q}_{aw} . In the current study we did not obtain a direct measurement of bronchial perfusion pressure, rather we estimated perfusion pressure from mean arterial pressure.

2.7. Statistical analysis

All data are presented as mean ± standard deviation (S.D.). The change in \dot{Q}_{aw} , from rest, to Load 1, Load 2 and back to rest were assessed using a repeated measures analysis of variance (ANOVA). Where a significant difference was found, Bonferroni *post hoc* tests were used to determine where this effect occurred. Relationships between \dot{Q}_{aw} and other dependent measures were evaluated using linear regression analysis. Statistical significance was set at $P < 0.05$.

3. Results

The metabolic, cardiovascular and \dot{Q}_{aw} responses measured at rest, during exercise and recovery are shown in Table 2. There was a significant, stepwise increase in both the measured metabolic ($\dot{V}O_2$, \dot{V}_E) and cardiovascular responses (HR, \dot{Q}_{tot} and mean arterial pressure) to exercise. Each of the measured metabolic and cardiovascular responses returned to pre-exercise levels during recovery.

We also found a significant, stepwise increase in \dot{Q}_{aw} during exercise at Load 1 and Load 2. \dot{Q}_{aw} returned pre-exercise levels during recovery. \dot{Q}_{aw} represented $130 \pm 7\%$ and $179 \pm 26\%$ of preexercise values during exercise at Load 1 and Load 2 respectively. Accompanying the stepwise increase in \dot{Q}_{aw} we found a progressive fall in BVR during exercise at Load 1 and Load 2 which returned to the pre-exercise levels during recovery.

Univariate correlation coefficients were calculated for the relationships between \dot{Q}_{aw} and \dot{Q}_{tot} , \dot{V}_E and $P_{ET}CO_2$. Significant univariate correlation coefficients ($P < 0.01$) were found for the relationship between \dot{Q}_{aw} and \dot{Q}_{tot} ($r = 0.58$) and between \dot{Q}_{aw} and \dot{V}_E ($r = 0.50$) (Fig. 2a and b respectively). No significant correlation was found between \dot{Q}_{aw} and $P_{ET}CO_2$ ($r = 0.24$, $P = 0.15$).

To determine the relative change in \dot{Q}_{aw} per unit change in cardiac output ($\dot{Q}_{aw}/\dot{Q}_{tot}$) we plotted $\dot{Q}_{aw}/\dot{Q}_{tot}$ vs \dot{Q}_{tot} (Fig. 3). The relative change in \dot{Q}_{aw} was inversely related to \dot{Q}_{tot} ($r = -0.44$, $P < 0.01$).

4. Discussion

This is the first study to examine simultaneous changes in \dot{Q}_{aw} , \dot{Q}_{tot} and \dot{V}_E during submaximal exercise in humans. Using noninvasive gas techniques to independently measure \dot{Q}_{aw} and \dot{Q}_{tot} , we found that \dot{Q}_{aw} increased during exercise and that these changes were related to the rise in both \dot{Q}_{tot} and \dot{V}_E .

We found that after approximately 10 min of submaximal exercise at Load 1 (34 W) \dot{Q}_{aw} had risen significantly and that an additional 10 min of exercise at a higher exercise intensity (68 W) resulted in a further rise in \dot{Q}_{aw} . In the present study, we examined changes in \dot{Q}_{aw} during submaximal exercise loads which could be best classified as being low to moderate (less than 80 W) intensity rather than heavy. We were unable to examine changes in \dot{Q}_{aw} at higher exercise intensities as subjects would have difficulty sustaining breath-holds for longer than 10 s under higher-intensity exercise conditions.

Our results suggest that the changes in airway circulation are related to changes in cardiac output during exercise (Fig. 2a). This result is similar to that of Elsasser et al. (1991) who reported a positive correlation between hypoxemia induced changes in \dot{Q}_{aw} and changes in \dot{Q}_{tot} in anaesthetized sheep. However when we examined the relative change in \dot{Q}_{aw} (i.e. the change in \dot{Q}_{aw} relative to the change in \dot{Q}_{tot}) the rise in \dot{Q}_{aw} during exercise tended to be less than the rise \dot{Q}_{tot} as shown by the inverse relationship between $\dot{Q}_{aw}/\dot{Q}_{tot}$ and \dot{Q}_{tot} (Fig. 3). Therefore, our results suggest that while there is an increase \dot{Q}_{aw} and \dot{Q}_{tot} during exercise, the proportion of \dot{Q}_{tot} which is directed towards the airways tends to decrease.

Hemodynamically, the rise in \dot{Q}_{aw} during exercise was due to both an increase in the perfusion pressure (as measured by an increase in mean arterial pressure) and a decrease in the BVR (Table 2). We did not obtain a direct measurement of bronchial perfusion pressure, which is estimated from the difference in mean arterial pressure and pulmonary artery pressure, i.e., bronchial perfusion pressure = mean arterial pressure – pulmonary artery pressure (Charan et al., 1998). However, given the low to moderate intensity of exercise employed in the current study, we would predict that the changes in PAP from rest to exercise would have been negligible (Stickland et al., 2004) and hence the approximation of perfusion pressure using the mean arterial pressure would be representative.

The fall in BVR (Table 2) suggests that there is a vasodilation of the bronchial vasculature during exercise. The vascular smooth muscle of the bronchial arteries has both α_1 and β_2 adrenergic receptors, with α_1 adrenergic receptors tending to predominate (Coleridge and Coleridge, 1994; Onorato et al., 1994; White et al., 2003). Brieva and Wanner (2001) showed

that inhalation of an α_1 receptor agonist resulted in an decrease in resting \dot{Q}_{aw} , while inhalation of a β_2 receptor agonist resulted in an increase. Apart from these adrenergic receptor mediated responses, there is evidence that \dot{Q}_{aw} is also regulated by shear stress and the release of endothelial related vasodilators (especially nitric oxide–NO) (White et al., 2003) and the release of local vasodilatory prostaglandins or neuropeptides associated with changes in local airway temperature (Baile et al., 1990).

Bronchial blood flow has been shown to be extremely labile and may be increased significantly by factors such as changes in temperature and hyperventilation (Coleridge and Coleridge, 1994). In the current study, we also found that the increase in \dot{Q}_{aw} was related to an increase in \dot{V}_E . Several animal studies have found a rise in \dot{Q}_{aw} associated with an increase in eucapnic hyperventilation (Baile et al., 1987, 1990; Parsons et al., 1989). In addition, hypercapnia has been associated with a marked increase \dot{Q}_{aw} (Baile and Pare, 1983). We measured P_{ETCO_2} as an indication of the changes in P_aCO_2 during exercise (Weinger and Brimm, 1987). During exercise there was a significant rise in the P_{ETCO_2} , however this small increase remained well within a normal range. Given this, it could be argued that as P_{ETCO_2} remained unchanged and that the ventilatory response in the current study was essentially eucapnic hyperpnoea.

In animal studies, the rise in \dot{Q}_{aw} in response to an increase in \dot{V}_E appears to be an important mechanism to maintain airway temperature and to mitigate airway cooling and drying (Parsons et al., 1989). During eucapnic hyperventilation at 20 and 40 l min⁻¹ with warm dry air in ventilated sheep, Parsons et al. (1989) showed there was a stepwise increase in \dot{Q}_{aw} . Similarly in humans, Kim et al. (1996) reported that eucapnic hyperventilation (40 l min⁻¹) with frigid air resulted in an increase in \dot{Q}_{aw} whereas the same level of ventilation with room air failed to result in any change in \dot{Q}_{aw} . These investigators concluded that the magnitude of change in increase in \dot{Q}_{aw} may reflect the magnitude of the thermal stress on the airway rather than the level of \dot{V}_E .

The temperature of the airway surface itself reflects a dynamic balance between heat loss (through evaporation, conduction and convection) and heat delivery by way of the bronchial circulation (Baile et al., 1985). Airway surface temperature will fall if there is an increase in heat loss through evaporation, conduction and convection without any concomitant increase in heat delivery by way of the bronchial circulation (i.e., an increase in \dot{Q}_{aw}). During exercise, increased airflow over the airway as a result of an increase in \dot{V}_E will result in greater evaporative and convective heat loss. In turn, \dot{Q}_{aw} would need to increase if the airway is to minimize the degree of cooling and drying that may occur during exercise (Parsons et al., 1989). Unfortunately the current study did not measure the temperature and humidity of the expired air during exercise and we acknowledge that further discussion on the change in airway surface temperature as a stimulus for the increase in \dot{Q}_{aw} during exercise remains beyond the scope of the current paper.

The results of the present study are in contrast to those reported by Bishop et al. (2007). These investigators found that \dot{Q}_{aw} , measured using a flowmeter mounted on the bronchial artery, decreased during moderate-intensity incremental exercise in four sheep. Bishop et al. (2007) also reported that airway diameter actually decreased during incremental exercise. These results were supported by a study by the same group (Quail et al., 2007) published at the same time. These studies (Bishop et al., 2007; Quail et al., 2007) concluded that at the onset of exercise there was a stimulus dependent constrictor effect in both the airway and the vascular beds.

The difference in these results to those of the present study may be due in part to the exercise protocol used to study changes in \dot{Q}_{aw} . Where we examined changes in \dot{Q}_{aw} during steady-state exercise, Bishop et al. (2007) used a rapid incremental protocol (i.e., 1-min exercise bouts)

consisting of short exercise bouts. These researchers have suggested that the rapid incremental protocol may have resulted in a constrictor rather than a dilatory response in both the airways and the vascular beds of the airways due to the fact that secondary factors such as thermal stress and the build up of metabolic by products of exercise that would have resulted in a dilation of the bronchial artery, may not have had time to take effect.

There are some limitations to the current study. Firstly the exercise intensities were low to moderate at best and we were unable to have subjects exercise at higher exercise intensities because of the breath holding requirement of the \dot{Q}_{aw} technique. Exercise at higher intensities may have provided information on whether \dot{Q}_{aw} continued to rise or plateaued at higher intensities. Secondly, given that we used a soluble gas technique to measure \dot{Q}_{aw} , there is the potential that the increase in \dot{Q}_{aw} may have been the result of an alveolar uptake of the DME. We believe this is unlikely as we were clearly able to define phase 1 of the expired N_2 washin curve in our analysis. Using this method we were clearly able to detect a DME concentration during expiration that excluded any alveolar gas mixing. In our validation of the technique we sampled the expired DME concentration earlier during the phase 1 expiratory phase (i.e. from a more proximal point in the deadspace) and we found that this did not significantly alter the measured \dot{Q}_{aw} . Thirdly we note that the sample size of 12 is small and may represent a limitation to the interpretation of our results. While we found that changes in \dot{Q}_{aw} , \dot{Q}_{tot} and V_E and the relationships between these changes were relatively homogenous during exercise, we acknowledge that a larger powered study would be warranted.

In conclusion, this study found a significant stepwise rise in \dot{Q}_{aw} with an increase in exercise intensity that was associated with an increase in both \dot{Q}_{tot} and V_E . Our results suggest that the increase in \dot{Q}_{aw} is mediated by both an increase in perfusion pressure and a decrease in BVR. The increase in \dot{Q}_{aw} may in turn be necessary to prevent excessive airway cooling and drying during exercise.

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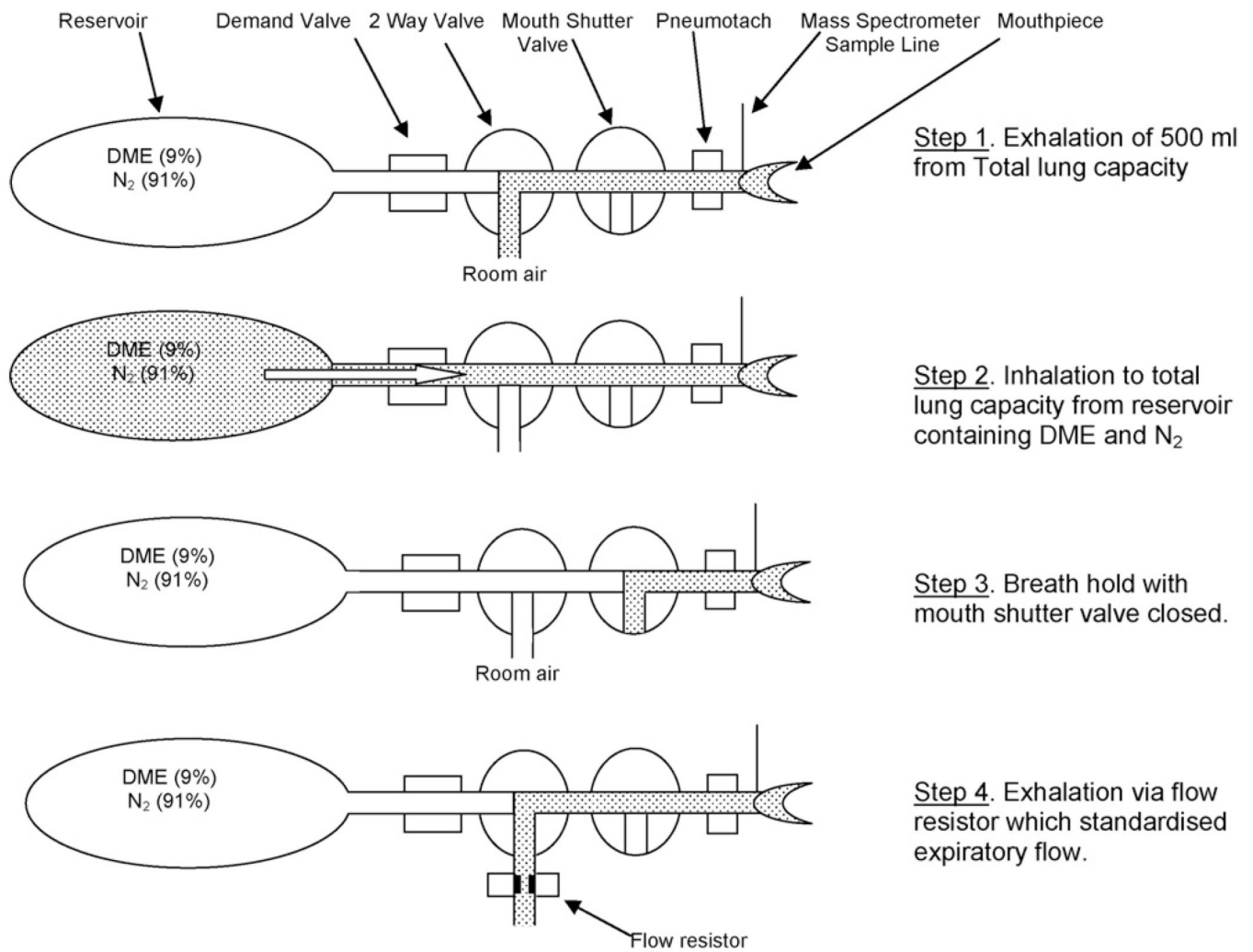


Fig. 1. Experimental apparatus and technique for measuring airway blood flow showing the four steps used both at rest and during exercise. Pneumotach: pneumotachometer; DME: dimethyl ether; N₂: nitrogen.

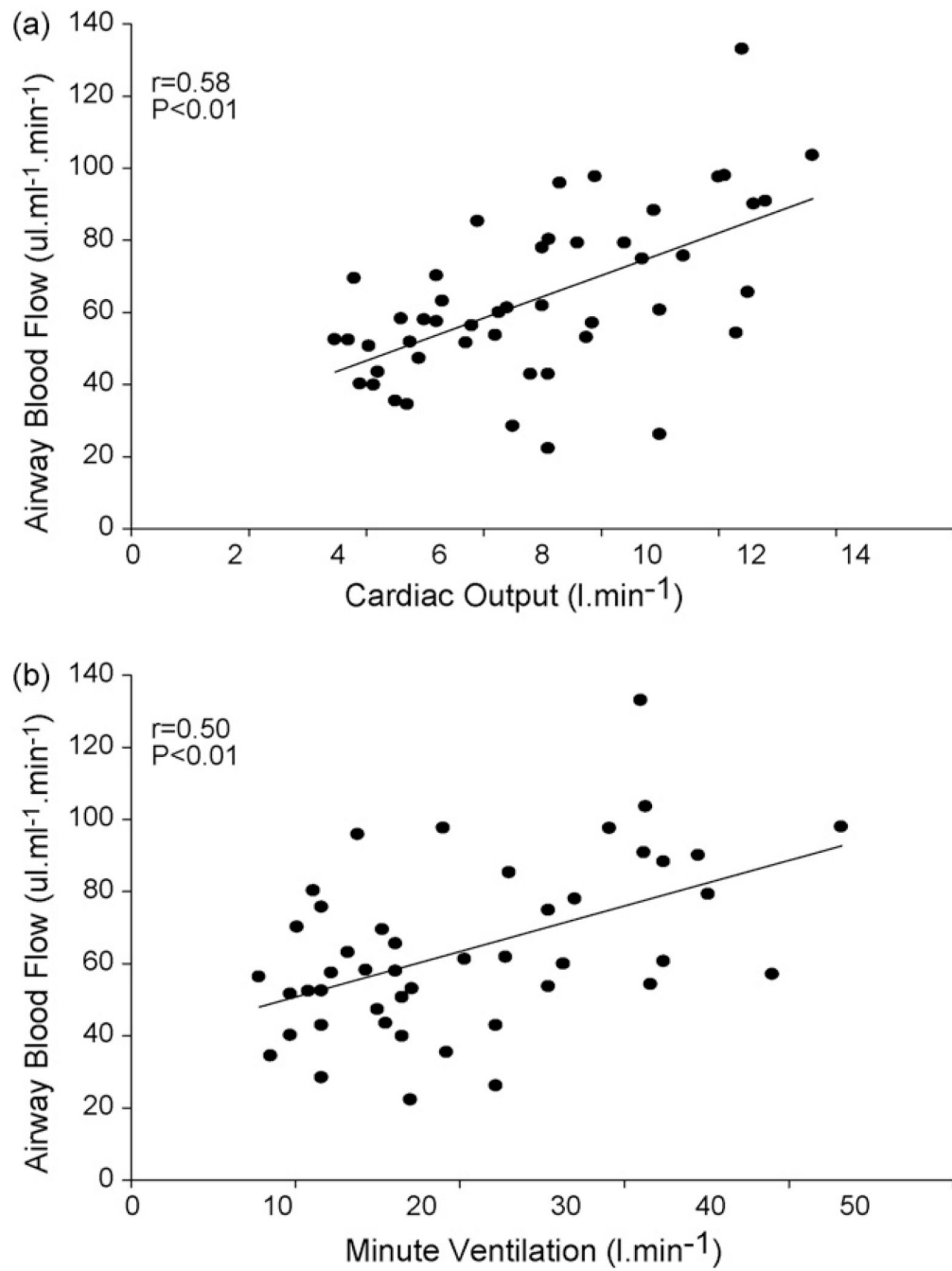


Fig. 2. Relationship between airway blood flow (\dot{Q}_{aw}) and cardiac output (\dot{Q}_{tot}) (a) and minute ventilation (\dot{V}_E) (b).

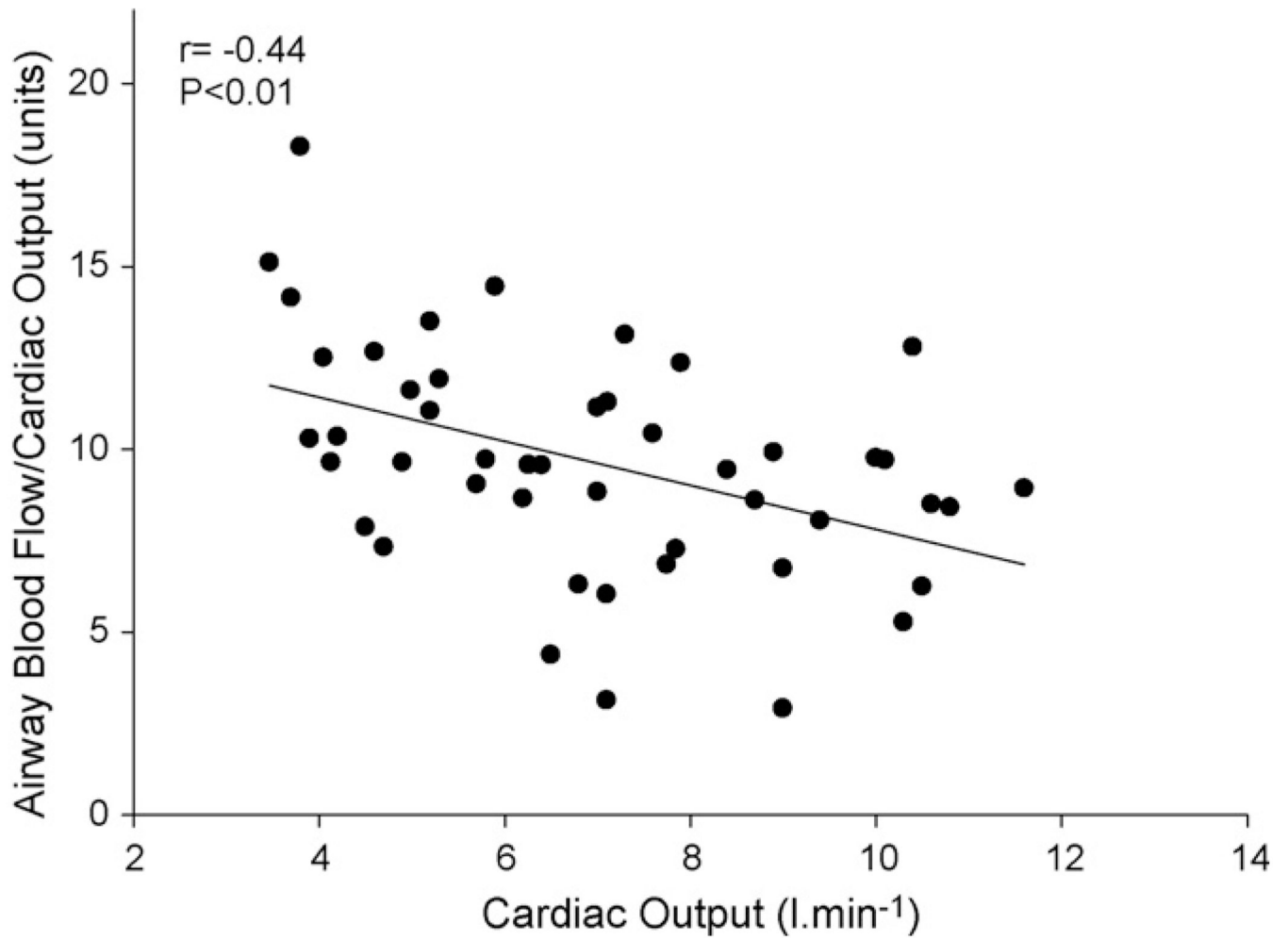


Fig. 3. Relationship between airway blood flow per unit cardiac output ($\dot{Q}_{aw}/\dot{Q}_{tot}$) and cardiac output.

Table 1

Physical characteristics, spirometry results and resting blood pressure of subjects

Age (yr)	34 ± 11
Male/female	5/7
BMI (kg m ⁻²)	24.3 ± 3.0
FEV ₁ (% predicted)	101 ± 11
FVC (% predicted)	101 ± 15
FEV ₁ /FVC (%)	84 ± 6
SBP (mmHg)	107 ± 9
DBP (mmHg)	66 ± 12

Values are mean ± S.D.; BMI: body mass index; FEV₁: forced expiratory volume in 1 s; FVC: forced vital capacity; SBP: systolic blood pressure; DBP: diastolic blood pressure.

Table 2

Physiological responses measured pre-exercise, during exercise and in recovery

	Pre-exercise	Load 1	Load 2	Recovery
Power (W)	Rest	34 ± 5	68 ± 10	Rest
VO ₂ (l min ⁻¹)	0.37 ± 0.08	0.92 ± 0.18*	1.32 ± 0.17*	0.41 ± 0.08
V _e (l min ⁻¹)	13.2 ± 3.6	22.4 ± 5.4*	32.2 ± 6.7*	13.9 ± 4.7
P _{ET} CO ₂ (mmHg)	33 ± 4	37 ± 3*	38 ± 4*	33 ± 3
HR (beats min ⁻¹)	74 ± 9	89 ± 8*	106 ± 9*	76 ± 13
Q _{tot} (l min ⁻¹)	5.3 ± 1.3	7.6 ± 1.2*	9.8 ± 1.3*	5.1 ± 1.1
MAP (mmHg)	80 ± 10	85 ± 9*	93 ± 9*	84 ± 10
Q _{aw} (μl ml ⁻¹ min ⁻¹)	52.8 ± 19.5	67.0 ± 20.3*	84.0 ± 22.9*	51.7 ± 13.2
BVR (units)	1.7 ± 0.7	1.4 ± 0.6*	1.2 ± 0.3*	1.7 ± 0.4

Results are mean ± S.D. VO₂: oxygen uptake; V_E: minute ventilation. P_{ET}CO₂: endtidal carbon dioxide; HR: heart rate; Q_{tot}: cardiac output; MAP: mean arterial pressure; Q_{aw}: airway blood flow. AVR (units): BVR (mmHg (μl ml⁻¹ min⁻¹)⁻¹).

* *P* < 0.05, different from pre-exercise mean.