Respiratory muscle dynamics and control during exercise with externally imposed expiratory flow limitation

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Aliverti, Andrea, Iacopo Iandelli, Roberto Duranti, Stephen J. Cala, Bengt Kayser, Susan Kelly, Gianni Misuri, Antonio Pedotti, Giorgio Scano, Paweł Sliwinski, Sheng Yan, and Peter T. Macklem. Respiratory muscle dynamics and control during exercise with externally imposed expiratory flow limitation. J Appl Physiol 92: 1953–1963, 2002. First published February 1, 2002; 10.1152/japplphysiol.01222.2000.—To determine how decreasing velocity of shortening (U) of expiratory muscles affects breath- ing during exercise, six normal men performed incremental exercise with externally imposed expiratory flow limitation (EFLex) at ~1 l/s. We measured volumes of chest wall, lung- and diaphragm-apposed rib cage (Vrc,p and Vrc,a, respectively), and abdomen (Vab) by optoelectronic plethysmo- graphy; esophageal, gastric, and transdiaphragmatic pressures (Pdi); and end-tidal CO2 concentration. From these, we calculated velocity of shortening and power (W) of diaphragm, rib cage, and abdominal muscles (di, rem, ab, respectively). EFLex forced a decrease in Uab, which increased Pab and which lasted well into inspiration. This imposed a load, overcome by preinspiratory diaphragm contraction. Udi and inspiratory Urem increased, reducing their ability to generate pressure. Pdi, Pem, and Wab increased, indicating an increased central drive to all muscle groups secondary to hypercapnia, which developed in all subjects. These results suggest a vicious cycle in which EFLex decreases Uab, increasing Pab and exacerbating the hypercapnia, which increases central drive increasing Pab even more, leading to further CO2 retention, and so forth.

muscle shortening velocity; respiratory failure; hypercapnia; ventilation; diaphragm; abdominal muscles; rib cage muscles; muscle power

WHEN A MUSCLE IS ACTIVATED, it develops force and/or shortens with a certain velocity. For a given degree of activation, the amount of drive converted into force and that converted to velocity are unique functions of the load the muscle is acting against and its own intrinsic force-velocity relationship. Against a resistive load, the velocity of shortening decreases as the resistance increases, but the force increases along the hyperbolic force-velocity relationship. This tends to maintain the muscle’s power output (the product of force and velocity), which changes less than either the velocity or the force alone. Provided that the muscle is not contracting isometrically and has a finite load, muscle power is therefore better than either pressure (e.g., occlusion pressure; Ref. 18) or flow (e.g., mean inspiratory flow; Ref. 16) if one wishes to obtain information about the central drive to breathe by measuring respiratory muscle mechanical output. Indeed, respiratory muscle power can be used as an approximate index of the central drive to the muscle (1).

We have shown that, in normal exercise, the dia- phragm is unloaded by relaxation of abdominal muscles throughout inspiration (1). This increases its shortening velocity so that it acts as a flow generator. Transdiaphragmatic pressure does not increase much, but diaphragmatic power increases with exercise in parallel with the increases in power of other respira- tory muscles, which develop the pressures required to displace the abdomen and rib cage and to inflate the lungs.

Having described the actions and control of respira- tory muscles during normal exercise (1), we aimed in the present research to determine how externally im- posed expiratory flow limitation (EFLex) affected exercise ventilatory pump performance. The experimental intervention we wished to achieve was a reduction in the velocity of expiratory muscle shortening; we then wished to measure its consequences. We, like Potter et al. (15), hypothesized that EFLex by decreasing expira-
To test our predictions, we have measured pressures, flows, and powers developed by the diaphragm, abdominal, and rib cage muscles during EFLe exercise. No reports exist in the literature on the three mechanical outputs of these muscle groups during EFLe exercise. We found that expiratory pressures and inspiratory flows did increase with a reduction in expiratory flow, but so did inspiratory pressures and the power developed by all three muscle groups.

METHODS

Subjects, measurements, and protocol. In this section, we focus on how we analyze our results to obtain pressures, shortening velocities, and power of various respiratory muscle groups. The experiments performed and the participating subjects were the same as reported in the companion paper (see Ref. 8 for details). In brief, we studied six healthy male subjects and measured the static deflation pressure-volume curve of the lung, the relaxation pressure-volume curve of the chest wall, flow at the mouth, end-tidal concentration of CO$_2$, esophageal (Pes) and gastric pressures (Pga), and chest wall volumes at rest and while exercising on a bicycle ergometer with workload increasing incrementally by 25 W every 4 min until exhaustion. Two exercise tests were performed on separate days, one with and the other without expiratory flow. We divided the chest wall into three compartments (1, 8, 17): the pulmonary or lung-apposed rib cage (RCp), the abdominal or diaphragm-apposed rib cage and the abdomen and measured their volumes (Vrc,p, Vrc,a, and Vab, respectively) by optoelectronic plethysmography (3). The border between the two rib cage compartments is approximated by a transverse section at the level of the xiphisternum, which corresponds to the upper border of the area of apposition. It was monitored continuously during EFLe exercise by ultrasound to make sure that the area of apposition did not shrink to the extent that the rib cage became a single compartment. Pes and Pga were measured by standard balloon catheter systems and used as indexes of pleural pressure and Pab. Transdiaphragmatic pressure (Pdi) was taken as Pga − Pes.

Vrc,p was plotted against pleural pressure during slow relaxation from total lung capacity (TLC) to functional residual capacity (FRC) to obtain the quasi-static pressure-volume curve of RCp. The pressure developed by rib cage muscles (Prcm) was measured as the distance along the pressure axis between the dynamic Vrc,p-pleural pressure loop and the relaxation curve. We did not correct these pressures for rib cage distortions that were <1% (8). What little distortion there was, was such that during control exercise Vrc,p was smaller than Vrc,a relative to the undistorted relaxed configuration, whereas during flow-limited exercise, Vrc,p was relatively larger. Therefore, we overestimated Prcm by 2–3 cm H$_2$O under control conditions and underestimated it by a similar amount during EFLe exercise (11).

Because abdominal muscle activity is absent during quiet inspiration (6), we used the relationship between inspiratory pressures developed by the abdominal muscles (Pab) and Vab at rest in addition to the curve measured during relaxation from TLC to FRC as the relaxation characteristic of the abdominal wall (1). Displacements of dynamic pressure-volume curves downward and to the right of this relationship were taken as evidence of abdominal muscle recruitment. Pab was measured as the distance along the pressure axis between the dynamic Vab-Pab loop and the abdominal wall relaxation line.

Analysis of abdominal dynamics. We plotted Pab vs. Vab during relaxation from TLC to FRC to obtain the relaxation curve of the abdominal wall. However, we observed that dynamic Pab-volume loops were frequently above and to the left of the relaxation line, particularly during the flow-limited runs. Although there are no known muscles that expand the abdominal wall directly, rib cage expansion must, through its mechanical linkage with the abdomen, expand at least that part of the abdomen that is directly subcostal. Rib cage abdominal coupling is measurable and positive; expansion of the rib cage facilitates expansion of the abdomen and vice versa (5). In Konno and Mead’s paper in which rib cage and abdominal displacements were measured at several different locations, a qualitative linkage between the subcostal abdominal wall and the rib cage can easily be discerned (see Fig. 5 in Ref. 12). In contrast to magnetometers and inductance plethysmography, optoelectronic plethysmography measures subcostal abdominal displacements and integrates these with the displacements of the rest of the abdomen to calculate the total volume swept by the abdominal wall. This method does not require the assumption that the abdomen behaves with a single degree of freedom. However, the rib cage abdominal coupling means that three agents act to displace the abdomen: Pab, rib cage, and abdominal muscles.

The actions of the rib cage and abdominal muscles can be expressed as pressures. When the chest wall is relaxed, there is no interaction between the rib cage and abdomen, and no pressure is developed by abdominal muscle contraction. Under these circumstances, the elastic recoil pressure of the abdomen (Pel,ab) balances Pab: Pel,ab = Pab. If the abdominal muscles remain relaxed and the chest wall departs from its relaxation configuration, Pab is no longer the only pressure determining the displacement of the abdominal wall because Pel,ab now balances an additional pressure resulting from the mechanical linkage between rib cage and abdomen. This can be expressed as a fraction of the pressures applied to the rib cage: Pel,ab = Pab + xPrc, where 0 < x < 1. Thus Vab will not be precisely predicted by Pab. If xPrc is positive, as when the rib cage-to-abdominal volume ratio is greater than during relaxation, Vab will be displaced above and to the left of the Vab-Pel,ab relaxation line. The distance from this point to the relaxation line along the pressure axis gives xPrc. If this situation is now combined with abdominal muscle contraction, Pel,ab = Pab + xPrc − Pabm. (The sign is negative because, although Pab is positive, its action is to make the abdomen smaller and thus decrease Pel,ab.) Under these circumstances, the distance along the pressure axis from a dynamic curve to the relaxation characteristic gives the difference of xPrc and Pabm. To solve for Pabm, one needs to know xPrc. As this is unknown, accurate measurement of Pab requires the use of a region of the abdomen where there is no interaction between it and the rib cage, i.e., where, despite departures of rib cage and abdomen from their relaxation configuration, Pel,ab = Pab + Pabm and xPrc = 0. We accomplished this by using the subumbilical region of the abdominal wall, where the influence of the rib cage was minimal, to calculate Pabm. Knowing Pab, one can solve for Pabm as the distance along the pressure axis between regional dynamic and regional relaxation curves.
To measure $P_{abm}$, we excluded the markers above the umbilicus and measured the relaxation curve of the rest of the abdominal wall by plotting its volume ($V_{ab}$) against $P_{ab}$.

An example is shown in Fig. 1A. We thus calibrated the effect of $P_{ab}$ alone on $V_{ab}$. Because $V_{ab}$ was unaffected by the rib cage, the horizontal displacement of the dynamic $V_{ab}$-$P_{ab}$ loop away from the relaxation line now quantified $P_{ab}$ in the usual way.

In one subject during control exercise, the motion of one of the markers was obscured. Although this made little difference in the calculation of $V_{ab}$, the error in regional $V_{ab}$ measurement was large so that we were unable to estimate $P_{ab}$ accurately. Thus we report mean values for $P_{ab}$ during control exercise in only five subjects. In another subject, the regional relaxation curves were not reproducible. Therefore, in this subject, we used the $P_{ab}$-$V_{ab}$ relationship during quiet expiration as the relaxation curve, as it is known that, in normal subjects, the abdominal muscles are usually relaxed during quiet breathing (6). In support of the assumption of relaxation, the quiet breathing $P_{ab}$-$V_{ab}$ loop was counterclockwise, whereas with expiratory muscle contraction, the loop is a figure eight.

Calculation of mean pressures, flows, shortening velocities, and power. As shown in Fig. 1B, expansion of $R_{cp}$ during exercise sometimes started when the dynamic pressure-volume loop was below and to the right of the $R_{cp}$ relaxation line. This figure is the most extreme example of this behavior. In other instances, this increase is mainly due to decompression of alveolar gas accompanying the fall in alveolar pressure at the end of expiration. Nevertheless, the method of calculating the distance along the pressure axis between the part of the dynamic loop to the left of the $R_{cp}$
relaxation line and the relaxation line (Prcm,i) does not allow for any measurement of Prcm,i during the initial expansion of RCp, although inspiratory rib cage muscles (RCMi) shorten during this period. We assumed (but do not have proof) that RCMi were activated at the onset of RCp expansion on the basis of our previous observation that expiratory muscles relax slowly during inspiration (1) so that inspiratory and expiratory muscles are coactivated. With coactivation of antagonistic muscle groups, muscle pressures developed are underestimated by Campbell-type diagrams. This is a source of error that, to the best of our knowledge, has not been addressed before. Thus, if coactivation occurred, the pressures we report for RCMi and expiratory rib cage muscles (RCMe) are minimal values and may in reality be somewhat greater.

Even if RCMi were relaxed when the dynamic Vrc,p-Pes loops were below and to the right of the relaxation line, RCMi started to shorten the instant RCp started to expand. Therefore, we estimated the mean flow generated by RCMi shortening as $\Delta V_{rc,p}/T_i$ and used this as an index of shortening velocity because RCMi pressure (Prcm,i) was not measurable until the dynamic Vrc,p-Pes loop crossed the static curve. Work was calculated as the area contained between the dynamic loop and the relaxation line from the time it crossed the relaxation line until Vrc,p reached its maximum. Any error resulting from this method of calculating work is similar to the error in calculating pressure. Values we report are minimum values and may in reality have been somewhat greater. We next calculated mean pressure by dividing work by the volume change used for the calculation of work. Rib cage muscle power was then calculated by multiplying mean flow by mean pressure.

The mean flow developed by the abdominal muscles was calculated in a fashion similar to RCMi, i.e., as $\Delta V_{ab}/$expiratory time, whereas the work during expiration was measured as the area between dynamic and relaxation curves between zero flow points. Mean pressure was calculated by dividing the work by $\Delta V_{ab}$ and abdominal muscle power was mea-

![Fig. 2. Ensemble averaged, mean values of pressures developed by rib cage muscles (Prcm), diaphragm (Pdi), and abdominal muscles (Pabm) during control (A) and EFLe exercise in the 4 subjects who hyperinflated (B) and the 2 subjects who did not hyperinflated (C). Each set of tracings shows the values averaged over the different subjects and over different respiratory cycles at each exercise workload. Each trace was obtained by 1) analyzing all breaths (measured at 100 Hz) during the final 40 s of each exercise workload in each subject; 2) normalizing each breath in time by resampling data (with linear interpolation) to obtain a fixed number of samples ($n = 500$) between the onset of inspiration and the end of expiration; 3) computing the ensemble average of Pdi, Prcm, and Pabm for each subject at each workload and expressing them as percentage of total respiratory cycle time (Ttot); and 4) averaging the data of all subjects at the same exercise level. Mean respiratory cycles are represented with the onset of inspiration at the left ordinate and the end of expiration at the right ordinate. The abscissa is percent of 1 complete respiratory cycle. ●, End-inspiratory points.](image-url)
sured as mean pressure × mean flow. Mean flow was used as an index of shortening velocity.

Vab was used as an index of diaphragm fiber length (2, 4) and ΔVab/Ti as mean velocity of diaphragmatic fiber shortening. The product (ΔVab/Ti)·ΔPdi was used as an index of diaphragmatic power, and fold increases in diaphragmatic power were calculated. ΔPdi was measured as peak inspiratory Pdi. The validity of this approach depends on the validity of the assumption that mean Pdi is in constant proportion to ΔPdi.

Statistics. To determine the significance of differences in various parameters between control and flow-limited exercise, we used the nonparametric Wilcoxon matched-pairs test.

RESULTS

EFLe markedly impaired exercise performance because of severe dyspnea. Dynamic hyperinflation was not a prominent feature of our results. In two of six subjects, it did not occur at all, and in the remaining four it only occurred at the end of the flow-limited run. Before that, during the Starling run, end-expiratory chest wall volumes were similar to or less than during control exercise, whereas dyspnea assessed by the Borg scale was considerably greater than at the same exercise level under control conditions. Ultrasound imaging of the area of apposition revealed little change in its area even with dynamic hyperinflation.

Respiratory muscle pressures. Figure 1 shows that there were marked increases of abdominal muscle, and inspiratory and expiratory rib cage muscle pressures during EFLe exercise compared with control. For all subjects, ensemble-averaged, instantaneous pressures developed by the diaphragm, rib cage, and abdominal muscles are shown in Fig. 2 under control and flow-limited conditions. The patterns of pressure development were quite similar between euvolumics and hyperinflators, although the former tended to have greater inspiratory pressures than the latter.

Figure 2 illustrates a number of features of EFLe exercise common to both euvolumics and hyperinflators: 1) there was a marked increase in expiratory Prcm and Pabm during the last two EFLe exercise workloads; 2) Ti shortened as exercise workload increased, whereas Prcm,i and Pdi increased; 3) at the onset of inspiratory flow, Pabm was positive, and this was exaggerated by EFLe exercise; 4) abdominal muscles relaxed slowly during much of inspiration; and 5) the diaphragm contracted before inspiration started to overcome the positive Pabm, as shown by the positive values of Pdi on the ordinates of Fig. 2. It is possible that RCMi were also recruited before inspiratory flow, but cocontraction of RCMi and RCMe cannot be demonstrated by Campbell-type diagrams; one would need to demonstrate electrical activity. The load imposed by inspiratory contraction of expiratory muscles diminished as abdominal muscles relaxed during inspiration. This led to an inspiratory fall in Pab.

Preinspiratory diaphragmatic contraction. Figure 3 shows individual results for the values of Pdi at the onset of inspiration as a function of workload during control

Fig. 3. Preinspiratory Pdi in each subject as a function of exercise workload. Letters in top left of each panel identify subjects. ○, Control; ●, EFLe exercise.
and EFLe exercise. There was considerable between-individual variation, but five of the six subjects showed increased preinspiratory Pdi during EFLe exercise, reaching a value as high as 40 cmH2O in subject II. During control exercise, preinspiratory Pdi never rose above 6 cmH2O. There was a similar broad between-individual variation in the values of Pabm at the onset of inspiration (data not shown). We are unable to explain the outlying preinspiratory Pdi of -3 cmH2O in MF, but he had the lowest expiratory muscle pressures of all subjects.

Determinants of diaphragmatic fiber length and shortening velocity. Figure 4 shows means ± SE of ΔVrc,a/ΔVab during control exercise in all six subjects and during flow-limited exercise in the hyperinflators and euvolumics separately. These data confirm our laboratory’s earlier observations that during control exercise ΔVrc,a/ΔVab is constant (1). This ratio did not change during EFLe exercise in either group and was similar to control exercise. Because diaphragmatic fiber length is determined by abdominal rib cage and abdomen (18), we used ΔVab as an index of change of diaphragmatic fiber length and ΔVab/Ti as an index of velocity of diaphragmatic shortening during both control and flow-limited exercise (1). We could not measure absolute diaphragmatic power in this way, but the fold increases could be compared with fold increases in power developed by other muscle groups.

Respiratory muscle velocity of shortening, force, and power. Figure 5 shows that, compared with control, EFLe decreased the flow generated by the abdominal muscles in all subjects, although the effect in MF was minimal.

Figure 6 shows mean ± SE values of powers generated, pressures developed, and indexes for shortening velocity of the abdominal and diaphragm muscles during control exercise and during flow-limited exercise in both groups. The data confirm our previous observations (1) that during control exercise abdominal and diaphragmatic powers were constant and similar to each other. EFLe decreased both powers, although the effect was minimal in MF (Fig. 5).

See text for further description.
ening velocities for RCMi, abdominal muscles, and diaphragm during control and flow-limited exercise. Expiratory muscle shortening velocity decreased whereas inspiratory muscle shortening velocity increased. Mean pressure and power of RCMi, abdominal muscles, and diaphragm all increased significantly.

Figure 7 illustrates pressure-to-velocity ratios. Compared with quiet breathing, this ratio fell for the diaphragm during both control and flow-limited exercise, and thus, during both forms of exercise, more of the central drive was converted into velocity of shortening and less into pressure as soon as exercise started. EFLe exercise did not change the ratio for RCMi but caused more of the central drive to abdominal muscles to be converted into pressure, as would be expected with the enforced slowing of shortening velocity.

End-tidal CO₂ concentration. End-tidal concentrations of CO₂ increased in all subjects at the highest level of EFLe exercise from a mean ± SE control value of 6.6 ± 0.3 to 7.9 ± 0.4% (P < 0.001), thus confirming earlier measurements (Ref. 9 and B. Kaysler, J. Suzuki, S. Yan, and P. T. Macklem, unpublished observations).

DISCUSSION

Critique of methods and main findings. Limitation of expiratory flow at an abnormally low level during exercise neutralizes the actions of expiratory muscles that are no longer able to increase expiratory flow rates simply by increasing alveolar pressure. Although, physiologically and pathophysiologically, flow limitation occurs in dynamically compressed intrathoracic airways, in our experiments the flow-limiting segment or choke point was the Starling resistor, and the tracheobronchial tree remained uncompressed. However, the mechanism of flow limitation was identical. It occurred when the velocity of airflow at the choke point reached wave speed.

Obviously, there are many other differences between exercise in patients with chronic obstructive pulmonary disease (COPD) and exercise in normal subjects with EFLe. These include loss of lung elastic recoil in COPD, inspiratory flow obstruction, alveolar wall and pulmonary capillary bed destruction, ventilation-perfusion mismatch and alterations in diaphragm mechanics due to chronic shortening, decreased area of apposition, and possible loss of sarcomeres, to name a few. These differences could certainly produce a different response to flow limitation during exercise than that which occurs in normal subjects. Nevertheless, we believe we have demonstrated important aspects of ventilatory pump dysfunction during flow-limited exercise and have shown that these lead to three of the

Fig. 5. Shortening velocity of abdominal muscles (ABM) in each subject expressed as ΔVab/expiratory time (Te) as a function of exercise workload. Letters in top left of each panel identify subjects. C, Control exercise; ●, EFLe exercise.
most important pathophysiological features of COPD, namely exercise limitation, severe dyspnea, and hypercapnia (Ref. 9 and Kayser et al., unpublished observations).

In the present experiments, we hypothesized that EFLe by decreasing expiratory muscle shortening velocity would increase expiratory muscle force. We predicted that this would increase shortening velocity of inspiratory muscles, thereby functionally weakening them. We succeeded in decreasing expiratory muscle flow and increasing expiratory muscle pressures.

Shortening velocity of the diaphragm was estimated by

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**Fig. 6.** A: group mean ± SE values for flows (velocity of shortening) of diaphragm muscles (right), RCMi (left), and ABM (middle) as a function of exercise workload. B: group mean ± SE values of pressures developed by RCMi (left), ABM (middle), and diaphragm (right) as a function of exercise workload. C: group mean ± SE values of RCMi (right), ABM (middle), and diaphragm (left) power relative to the power at zero workload as a function of exercise workload. ○, Control exercise; ●, EFLe exercise. *P = 0.05; **P = 0.02.

**Fig. 7.** Group mean ± SE values of pressure-to-velocity ratios of RCMi (left), ABM (middle), and diaphragm (right) as a function of exercise workload. ○, Control exercise; ●, EFLe exercise. *P = 0.05; **P = 0.02.
The displacement of abdominal rib cage in addition to Vab is also an important determinant of diaphragmatic fiber length (14), although recent evidence suggests that its role may be overestimated (2, 4). Be that as it may, as long as $\Delta V_{rc,a}/\Delta V_{ab}$ is constant (Fig. 4), $\Delta V_{ab}/T_i$ can be used as an index of diaphragmatic shortening velocity and the product $(\Delta V_{ab}/T_i) \cdot \Delta P_{di}$ as an index of diaphragmatic power (1). $\Delta V_{ab}/T_i$ and $R_{CMi}$ flow were increased by EFLe. We interpret this as validating our hypotheses and that the increased shortening velocity of inspiratory muscles functionally weakened them.

Effects of decreasing expiratory muscle-shortening velocity. Remarkably, in a landmark paper published thirty years ago, Potter et al. (15) described high values of expiratory pressure during exercise in patients with COPD and also attributed these to a reduction in velocity of shortening of expiratory muscles. They postulated that the increased pressures might decrease venous return and demonstrated an association between the increase in expiratory pressure and dyspnea. Clearly they anticipated many of our results.

If the effects of a decrease in shortening velocity were only to increase force development and the increase in force had no further effects, one might expect little change in expiratory muscle power. However, both $R_{CMi}$ (data not shown) and abdominal muscle power increased (Fig. 6). Furthermore, both $P_{di}$ and $P_{rcm,i}$ increased despite a decrease in their ability to generate force, resulting from an increase in their shortening velocity (Fig. 6). Thus we conclude that central drive to all respiratory muscles increased during EFLe exercise. Presumably the increase in partial pressure of CO$_2$ is an important reason for this. The increase in expiratory pressures resulting from the decrease in velocity of shortening was also responsible for the blood shifts from trunk to extremities that we measured (8). The role of high expiratory pressures and blood shifts in producing hypercapnia has been discussed elsewhere (Ref. 8 and Kayser et al., unpublished observations).

Despite the changes in force, shortening velocity, power, and central drive, the pressure-to-flow ratios shown in Fig. 7 were unchanged for the diaphragm; they fell from rest to exercise. Thus a greater fraction of the power was converted to flow, and the diaphragm maintained its normal role as a flow generator (1), although it developed the pressure to overcome the persistent abdominal muscle contrac-

![Graphs and equations](image)

**Fig. 8.** Individual regressions of the change in pressure developed by ABM from control to externally imposed EFLe exercise ($\Delta P_{abm}$) at the same workload vs. the change in fraction of end-tidal CO$_2$ concentration ($\Delta F_{ETCO_2}$) in the five subjects in whom we were able to measure $P_{abm}$. Regression equations and significance levels are shown at bottom right. Letters in top left of each panel identify subjects.
tion at the onset of inspiration. Similarly, the pressure-to-flow ratios of the other inspiratory muscles were not influenced by EFLe, and RCMi continued to displace the rib cage (1) by increasing their pressures to compensate for the increase in flow. EFLe exercise only influenced the pressure-to-flow ratio for the abdominal muscles.

Abdominal muscle-diaphragm interactions. Normally in exercise, the abdominal muscles relax gradually throughout inspiration (1). Their contraction at the onset of inspiratory effort imposes a load in the form of an expiratory pressure that the inspiratory muscles must overcome to initiate inspiratory flow. Furthermore, as abdominal muscles gradually relax during inspiration, the load is evanescent and disappears by end inspiration. We failed to appreciate this in our laboratory’s previous paper (1). Normally this load is relatively small (Fig. 3) and is easily overcome probably by passive stretching of the diaphragm secondary to inward abdominal displacement and abdominal muscle recruitment. If so, the gradual relaxation costs little as the load it imposes is overcome by elastic energy stored in the diaphragm. We do not have proof that this Pdi is passive, which would require the measurement of the diaphragmatic electrical activity. However, Goldman and Mead (7) demonstrated a passive Pdi with abdominal compression of a similar magnitude to that in the present work.

This mechanism fails to work in EFLe exercise due to the marked increase in Pab and because the inward abdominal displacements were less during EFLe exercise (8), producing less diaphragm stretching. Pabm was too great for a passive Pdi to overcome, and active diaphragm contraction was required to initiate inspiratory flow. When this load is combined with dynamic hyperinflation, the total load is the sum of that imposed by so-called intrinsic positive end-expiratory pressure and that due to expiratory muscle pressure. Thus the hyperinflators had to overcome both loads. In this regard, Lessard et al. (13) found that, in mechanically ventilated patients, expiratory muscle activity increased intrinsic positive end-expiratory pressure independently of dynamic hyperinflation.

Role of CO2. In studying the effects of EFLe exercise, we have consistently observed an increase in end-tidal PCO2 levels as high as 65 Torr. In a limited number of subjects, we have confirmed that the elevated end-tidal values represent arterial hypercapnia in part resulting from an increased alveolar dead space (Kaysen et al., unpublished observations), possibly resulting from blood shifts from thorax to extremities secondary to the high intrathoracic pressure and Pab (8).

The increase in arterial partial pressure of CO2 presumably increases the drive to all respiratory muscles so that expiratory muscles develop even greater pressure than that resulting from the reduced velocity of shortening. Breathing resembles Valsalva’s maneuver (8), but whether or not this results in a decreased cardiac output remains to be determined. We have been unable to find any references to the effects of Valsalva’s maneuver during exercise. However, the combination of hypercapnia, a possible reduction in cardiac output, increased drive to all respiratory muscles, and decreased ability of inspiratory muscles to develop force because of their increased shortening velocity, all conspire to impair ventilatory pump function and exercise performance. This scenario implicates the decrease in velocity of shortening of expiratory muscles as the primary initiating event that ultimately results in a remarkable number of pathophysiological effects.

To investigate the interrelationships between expiratory pressures, hypercapnia, and increased respiratory drive further, we regressed the difference between control and EFLe abdominal muscle pressure as the independent variable against the difference in fractional concentration of end-tidal CO2 as the dependent variable. Regression lines were drawn for each individual at all levels of exercise. The results are shown in Fig. 8. This confirmed the significant relationship (P < 0.0001) found by Kaysen et al. (unpublished observations) between end-tidal Pco2 and peak expiratory Pes. The differences in end-tidal concentration of CO2 as the independent variable were then regressed against the differences from control to EFLe exercise in diaphragmatic power as the dependent variable. This was also statistically significant (P < 0.005). We conclude that whereas no proof exists for our speculation, there is sufficient evidence to support it as a reasonable hypothesis worthy of future investigation. It would be important to know whether this unfortunate sequence of events occurs in obstructive airway disease.

REFERENCES


