Similar ventilation distribution in normal subjects prone and supine during tidal breathing

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Rodríguez-Nieto, M. J., G. Peces-Barba, N. González Mangado, M. Paiva, and S. Verbanck. Similar ventilation distribution in normal subjects prone and supine during tidal breathing. J Appl Physiol 92: 622–626, 2002; 10.1152/japplphysiol.00574.2001.—Multiple-breath washout (MBW) tests, with end-expiratory lung volume at functional residual capacity (FRC) and 90% O2, 5% He, and 5% SF6 as an inspired gas mixture, were performed in healthy volunteers in supine and prone postures. The semilog plot of MBW N2 concentrations was evaluated in terms of its curvilinearity. The MBW N2 normalized slope analysis yielded indexes of acinar and conductive ventilation heterogeneity (Verbanck S, Schermans D, Van Muylem A, Paiva M, Noppen M, and Vincken W. J App Physiol 83: 1907–1916, 1997). Also, the difference between SF6 and He normalized phase III slopes was computed in the first MBW expiration. Only MBW tests with similar FRC in the prone and supine postures (P > 0.1; n = 8) were considered. Prone and supine postures did not reveal any significant differences in curvilinearity, N2 normalized slope-derived indexes of conductive or acinar ventilation heterogeneity, nor SF6-He normalized phase III slope difference in the first MBW expiration (P > 0.1 for all). The absence of significant changes in any of the MBW indexes suggests that ventilation heterogeneity is similar in the supine and prone postures of normal subjects breathing near FRC.

ventilation heterogeneity; tidal breathing; posture; phase III slope

SINCE THE WORK of Piehl and Brown (15), showing improved gas exchange in patients when they are positioned in the prone posture, several authors have confirmed these findings (5). The exact reason for improved gas exchange remains uncertain, but it is most often sought in the redistribution of lung ventilation, perfusion, or both. Research into the actual beneficial effect of prone ventilation is hampered by the many confounding factors that can affect the study outcomes. For instance, Tokics et al. (19) have shown that, in supine, anaesthetized, mechanically ventilated patients, nondependent lung regions receive a larger fraction of the inhaled volume, in contrast to what is observed in awake normal subjects. Also, the lung volume at which measurements of perfusion and/or ventilation are done in supine and prone postures will affect the results, yet the actual lung volumes with the test subjects supine and prone are rarely reported.

Whereas Kaneko et al. (9) had suggested that the pleural pressure gradient does not change between prone and supine postures, a recent study by Mayo et al. (11), using magnetic resonance imaging in humans, estimated that the pleural pressure gradient is three times smaller prone than supine. Potential differences of top-to-bottom ventilation distribution could also be linked to the different location of the heart with respect to the portion of the dependent lung regions that it is compressing (1). In the prone posture, the heart is seen to be mainly resting on the sternum, whereas a considerable portion of the left lung is compressed by its location underneath the heart when supine. The gravity-dependent effect on ventilation distribution in the different postures has been most widely assessed in terms of lung imaging. For instance, Amis et al. (2) monitored two Krypton gas isotopes with very different half-lives in 12 normal male humans to suggest that both ventilation-to-alveolar volume ratio and regional functional residual capacity (FRC)-to-regional total lung capacity (TLC) ratio were more uniform prone than supine.

We have shown recently (16) from vital capacity single-breath washouts that, of all recumbent postures, the prone posture most reduces ventilatory inhomogeneities. However, vital capacity tests are particularly sensitive to events occurring near residual volume and TLC (6) and are not representative of ventilation distribution during tidal breathing. We have, therefore, decided to perform multiple-breath washouts (MBW) in prone and supine postures. The MBW test has been previously shown to be sensitive to alterations in ventilation distribution and to enable the separation between mechanisms leading to ventilation inhomogeneities in the conductive and acinar airway compartment of the lungs (4, 20). We hypothesized

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that, by using these MBW-derived indexes of ventilation distribution, we could detect any possible changes in ventilation distribution between supine and prone postures.

MATERIALS AND METHODS

The experimental system was identical to that previously used for single-breath washout measurements (16). Briefly, it consisted of a cylindrical cage accommodating a stretcher that could rotate around its longitudinal axis while allowing gas concentration and volume measurements during breathing experiments. The stretcher was equipped with a leather holding garment covering only the anterior rib cage, like a cuirass, and leather straps over the waist and ankles to keep the subject in a steady posture for any rotational position of the stretcher. The garment minimized pressure on the abdominal region and kept the subject comfortably suspended in the prone posture.

A mouthpiece connected the subject to the breathing assembly, incorporating a bag-in-box system, containing inspiratory and expiratory 40-liter meteorological balloons, a pneumotachograph in its wall (series 3700, Hans Rudolph, Kansas City, MO), and a pressure transducer (Poch-Millas, I+D, Madrid, Spain). A mass spectrometer (MGA1100, Marquette, Milwaukee, WI) capillary continuously sampled gas at ~1 ml/s in front of the subject’s mouth, and total dead space amounted to 42 ml. Data acquisition of gas and volume data at 1,000 Hz was handled by Testpoint software (Billerica, MA) using a 12-bit analog-to-digital card (Keithly Metrabyte, Taunton, MA). All 1,000-Hz gas concentration and volume signals were run through a software median filter and subsampled at 100 Hz for further analysis.

Twelve normal subjects participated in this study and performed three MBW tests in both supine and prone postures, using 90% O2, 5% He, and 5% SF6 as a test gas mixture. All subjects inhaled 1 liter, starting from their FRC, in each posture. Final selection of subjects and tests was done after a posteriori on the basis of the FRC values calculated from MBW analysis. To be included in the data set, subjects had to have two valid MBW tests with FRC that did not differ by >10% between each posture and with average FRC in each posture that did not differ by >10% between supine and prone. In this way, eight subjects (3 women, 5 men) could be included for further analysis.

MBW data were analyzed as in previous studies (4, 20). The MBW tests were first used to determine FRC and Fowler dead space of the first breath. Then N2 concentration was plotted as a function of volume in each expiration, where N2 phase III slope was computed and normalized by the corresponding mean expired N2 concentration. Plotting normalized slope (S) vs. lung turnover (TO) (cumulative expired volume over FRC) resulted in progressively increasing S as a function of lung TO. Indexes of conductive airway heterogeneity (Scond) and acinar airway heterogeneity (Sacin) are then derived as follows. Scond is defined as the regression slope of S vs. TO in the part of the MBW in which only conductive airways are contributing to the slope of ln S, i.e., between TO = 1.5 and TO = 6. Sainc is determined by subtracting, from the S value of the first breath, the part that is attributed to the conductive airways, i.e., Scond multiplied by the TO value of the first breath.

In the first breath of the MBW, we also computed the difference between SF6 (SSF6) and He (SH2) normalized phase III slopes [(SSF6 − SSH2)/n − 1] as an index of intra-acinar ventilation heterogeneity, similar to what is done in the case of single-breath washout tests (16). Based on the fact that SH2 and SSH2 are predominantly representative of proximal and peripheral intra-acinar airways, respectively, a differential response of SH2 and SSH2, i.e., a change in (SSF6 − SSH2/n − 1), due to a postural change would indicate structural changes occurring at different intra-acinar lung levels.

Finally, the decreasing N2 concentration in successive expirations is used for an additional MBW-derived index of ventilation distribution (20) as follows. In the semilog plot of mean expired N2 concentration as a function of TO, the curvilinearity (Curv) is computed as the ratio of the regression slope between TO = 3 and TO = 6 and the regression slope between TO = 0 and TO = 3. In fact, Curv = 1 represents a homogeneously ventilated lung, but, even in normal subjects, Curv is always <1 (a more curvilinear N2 washout curve leads to a smaller value for Curv). Curv was computed as a complement to Scond because it can represent ventilation differences between convection-dependent lung units, i.e., subventing from the conductive airways, even when these units empty synchronously. This contrasts with Scond, which requires asynchronous emptying to reveal existing concentration differences between these units.

Unless stated otherwise, all results are expressed as means ± SD. All pairwise comparisons are intra-subject comparisons for which we used Wilcoxon rank tests, accepting significance at P < 0.05.

RESULTS

Table 1 shows the breathing parameters pertinent to the interpretation of ventilation distribution tests such as the MBW: tidal volume (VT), FRC, and breathing frequency. In particular, Table 1 contains the data obtained from the eight subjects included in this study on the basis of their similar FRC value prone and supine (P > 0.1). In addition, breathing frequency and VT were also seen not to differ between both postures (P > 0.1). The mean ± SD values of all ventilation distribution indexes derived from the MBW test are summarized in Table 2, and none of these were significantly affected by the postural change between supine and prone (P > 0.1 for all).

<p>| Table 1. Subject characteristics and breathing parameters in supine vs. prone postures |
|---------------------------------|--------|--------|-----------|--------|--------|-----------|--------|--------|-----------|</p>
<table>
<thead>
<tr>
<th>Age, yr</th>
<th>Height, cm</th>
<th>Weight, kg</th>
<th>VT, liters</th>
<th>FRC, liters</th>
<th>Breathing Frequency, breaths/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine</td>
<td>Prone</td>
<td>Supine</td>
<td>Prone</td>
<td>Supine</td>
<td>Prone</td>
</tr>
<tr>
<td>Mean</td>
<td>37</td>
<td>172</td>
<td>72</td>
<td>0.98</td>
<td>0.98</td>
</tr>
<tr>
<td>SD</td>
<td>10</td>
<td>7</td>
<td>13</td>
<td>0.07</td>
<td>0.07</td>
</tr>
<tr>
<td>P</td>
<td>&gt;0.1</td>
<td>&gt;0.1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VT, tidal volume; FRC, functional residual capacity. P values were obtained from Wilcoxon paired t-tests between supine and prone.

J Appl Physiol • VOL 92 • FEBRUARY 2002 • www.jap.org
VENTILATION DISTRIBUTION IN RECUMBENT BODY POSTURES

Table 2. Multiple-breath washout results in supine vs. prone postures

<table>
<thead>
<tr>
<th></th>
<th>$S_{\text{acin}}$, liter$^{-1}$</th>
<th>$S_{\text{cond}}$, liter$^{-1}$</th>
<th>$(S_{\text{SF6}} - S_{\text{He}})$, liter$^{-1}$</th>
<th>Curv</th>
<th>V09, ml</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Supine</td>
<td>Prone</td>
<td>Supine</td>
<td>Prone</td>
<td>Supine</td>
</tr>
<tr>
<td>Mean</td>
<td>0.153</td>
<td>0.143</td>
<td>0.035</td>
<td>0.028</td>
<td>0.084</td>
</tr>
<tr>
<td>SD</td>
<td>0.047</td>
<td>0.057</td>
<td>0.013</td>
<td>0.016</td>
<td>0.047</td>
</tr>
<tr>
<td>$P$</td>
<td>&gt;0.1</td>
<td>&gt;0.1</td>
<td>&gt;0.1</td>
<td>&gt;0.1</td>
<td>&gt;0.1</td>
</tr>
</tbody>
</table>

$S_{\text{acin}}$ and $S_{\text{cond}}$ N$_2$ normalized slope derived indexes of acinar and conductive ventilation inhomogeneity, respectively; $(S_{\text{SF6}} - S_{\text{He}})$, slope minus He slope of the first multiple-breath washout breath; Curv, curvilinearity of semilog N$_2$ washout concentrations; V09, Fowler dead space of the first multiple-breath washout N$_2$ expiration. $P$ values were obtained from Wilcoxon paired t-tests between supine and prone.

DISCUSSION

This study shows that, under well-controlled conditions of lung volume, $V_t$, and breathing frequency (Table 1), no changes can be observed on any of the MBW-derived indexes of ventilation heterogeneity in the prone vs. supine posture (Table 2). In particular, ventilation heterogeneity in the acinar and conductive airway compartments, as reflected in $S_{\text{acin}}$ and $S_{\text{cond}}$, respectively, remained unchanged between the supine and prone postures. In addition, an index of acinar ventilation heterogeneity \( [(S_{\text{SF6}} - S_{\text{He}})_{n+1}] \), which would have been modified if different structural changes were taking place at different levels within the acini, remained unchanged between supine and prone postures. Hence, our previous observation of \( S_{\text{SF6}} - S_{\text{He}} \) increase in prone vs. supine posture for a vital capacity single-breath washout (16) was probably due to postural-dependent modifications near residual volume and/or TLC (6). The Curv of the MBW mean expired concentration semilog plot, which would indicate different relative expansions of lung units larger than acini, even in the absence of asynchronous emptying, was similar supine and prone. Finally, no posture-dependent change in anatomical dead space was observed.

The present results may seem surprising, considering the extensive literature on animal studies generally suggesting that the distribution of ventilation is more uniform in the prone position (7, 10, 12). We have previously shown that, both in steers (17) and in rats (21), mechanisms of ventilation distribution may actually be quite different from those observed in humans. For instance, human lungs display a pattern of flow asynchrony between convection-dependent lung units that seems to be absent in both steers and rats (17, 21).

As the reasons for the different behavior of human lungs from those species are not clear, we decided to relate our MBW data to previous reports on ventilation distribution in humans only.

Most previous reports in the literature of ventilation or perfusion distribution in humans supine and prone were derived from imaging studies, with results that may depend on the technique used, the part of the lungs in which the regions of interest were defined, and the lung volume at which measurements were made. For instance, Verschakelen et al. (22) found gradients in computed tomography (CT) lung density between dependent and nondependent lung regions that were most marked at low lung volumes, without, however, observing any difference in density gradients between supine and prone postures. Because the observed regional differences in CT lung densities were explained by gravity-dependent differences in perfusion and lung inflation, the similar pattern observed supine and prone would suggest either that perfusion and ventilation gradients between dependent and nondependent were similar prone and supine, or that both the perfusion and ventilation gradients are reduced in the prone vs. supine posture. A more recent electron-beam CT study by Jones et al. (8) did not find a difference in gravity-dependent perfusion gradient between supine and prone postures, but density of lung parenchyma was found to be more uniform in the prone posture. Measured at end-inspiration of mechanically ventilated healthy subjects with a 890- to 980-ml $V_t$ above FRC, these data were suggested to reflect a more evenly distributed ventilation in the prone posture. Using two Krypton isotopes with a 13-s and 4.4-h half-life, Amis et al. (2) found that both ventilation-to-alveolar volume ratio and regional FRC-to-regional TLC ratio were more uniform prone than supine. Our MBW data suggest that the associated attenuation of ventilation heterogeneity in the prone vs. supine posture is probably marginal in the near-tidal breathing range.

Considering only the data on spontaneously breathing human subjects, the divergence of reports reviewed by Mure and Lindahl (13) is related most to ventilation results obtained supine vs. prone. Perfusion results, also obtained with widely varying imaging techniques, are more coherent in showing a preferential perfusion of the dependent vs. nondependent lung regions supine, which is attenuated prone. Using magnetic resonance imaging performed at TLC, Stock et al. (18) found a reversal and an attenuation of the perfusion gradient between dependent and nondependent lung zones on turning normal subjects from supine to prone. A single-photon-emission CT study of intravenously injected radiolabeled albumin macroaggregates by Nyren et al. (14) displayed a marked top-to-bottom gradient of pulmonary perfusion in supine, spontaneously breathing subjects, only in the diaphragmatic lung section and not in the apical and intermediate lung sections. However, even in the diaphragmatic lung section, Nyren et al. did not find a perfusion gradient with the same healthy subjects prone. If we may assume that, in our subjects, perfusion gradients were also attenuated prone, whereas ventilation gra-
dients remained largely unaffected, as inferred from our MBW data, this would predict a better ventilation-perfusion match (because of the larger perfusion than ventilation gradient in normal humans).

The lung volume at which any measurement of lung function or ventilation-perfusion distribution is made is crucial for the comparison of supine and prone postures. Although the beneficial effect on oxygenation of the prone positioning has also been attributed to an increased FRC, several studies with unmodified FRC, yet improved oxygenation, contradict this hypothesis (13). Although it is generally assumed that FRC increases in the prone vs. supine posture, actual values of FRC changes vary widely (5), depending also on the extent to which the abdomen is supported or whether normal subjects or, for instance, acute respiratory distress syndrome patients are considered. In the present study, we deliberately selected only MBW tests performed with similar FRC supine and prone, which is mandatory for a valid interpretation of MBW results (3). Under these circumstances of similar FRC (Table 1), ventilation distribution was found to be similar prone and supine.

It is possible that the MBW test was, in fact, unable to pick up a subtle change in ventilation heterogeneity between prone and supine postures. Let us consider here the MBW indexes representing large-scale ventilation distribution, which may, at least in part, also become visible by means of lung imaging techniques: Curv and S_{cond}. In theory, a change in distribution of specific ventilation between convection-dependent lung units affects Curv. A change in distribution of specific ventilation and/or a modified pattern of flow asynchrony between these lung units affects S_{cond}. Hence, we could speculate that changes in ventilation distribution may have occurred between lung units that empty synchronously. Indeed, such changes may have been too subtle to be detected by Curv and, in the absence of associated flow asynchrony, undetectable by S_{cond}. Finally, whereas phase III slope analysis of the MBW test is the subject of alternative interpretations based on purely convection-dependent lung units (23), the experimental data that form the basis for any such interpretation do not show any significant differences between the prone and supine postures.

Finally, each interpretation of ventilation distribution data is implicitly associated with specific models and experiments. Even though the most common concept of ventilation distribution is a frequency distribution of the number of regions with a given rate of ventilation, we favor the use of the MBW to assess ventilation distribution because it can provide a link with the anatomical lung units between which ventilation heterogeneities occur. In particular, it can distinguish between ventilation heterogeneities originating in the acinar and conductive airways (20). Another concept is the spatial distribution of ventilation, but this would require imaging techniques that we have not used in the present study.

In summary, we have used a noninvasive, indirect measure of ventilation distribution during near-tidal breathing with a similar FRC supine and prone to conclude that there were no significant differences in any of the indexes of ventilation heterogeneity between prone and supine postures.

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