Lung Ventilation and Perfusion in Prone and Supine Postures with Reference to Anesthetized and Mechanically Ventilated Healthy Volunteers

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ABSTRACT

Background: The literature on ventilation (V) and lung perfusion (Q) distributions during general anesthesia and controlled mechanical ventilation in supine and prone position is contradictory. The authors aimed to investigate whether V, Q, and ventilation to perfusion ratio (V/Q) matching in anesthetized and mechanically ventilated volunteers are gravity dependent irrespective of posture.

Methods: Seven healthy volunteers were studied at two different occasions during general anesthesia and controlled mechanical ventilation. One occasion studied ventral to dorsal V and Q distributions in the supine posture and the other in the prone posture. Imaging was performed in supine posture at both occasions. A dual radiotracer technique and single photon emission computed tomography were used. V and Q were simultaneously tagged with 99mTc-TechneScan labeled macroaggregates of human albumin (TechneScan LyoMAA, Mallinckrodt Medica, Petten, The Netherlands) and 113mIn-mastebbega (Tetley Manufacturing Ltd., Sydney, Australia) and 113mIn-labeled macroaggregates of human albumin (TechneScan LyoMAA, Mallinckrodt Medica, Petten, The Netherlands), respectively.

Results: No differences in V between postures were observed. Q differed between postures, being more uniform over different lung regions in prone posture and dependent in supine posture. The contribution of the vertical direction to the total V/Q ratio heterogeneity was larger in supine (31.4%) than in prone (16.4%) (P = 0.0639, two-tailed, paired t test) posture.

Conclusions: During mechanical ventilation, prone posture favors a more evenly distributed Q between lung regions. V distribution is independent of posture. This results in a tendency toward lower V/Q gradients in the ventral to dorsal direction in prone compared with supine posture.

IN 1991, Glenny et al. 1 stated that gravity is a minor determinant of pulmonary blood flow distribution. This publication challenged the existing dogma of gravity-dependent lung perfusion. 2 At about the same time, the question of positioning patients supine or prone while treating for acute lung insufficiency was revitalized. 3–8 A complete understanding of the complex interactions between lung perfusion and ventilation has not been reached, although a recent publication discovered a higher expression of nitric oxide synthase in dorsal parts of human lung compared with ventral parts, indicating a role of nitric oxide in directing lung blood flow. 9

What We Already Know about This Topic

Diamond

Oxygenation improves in some patients with acute lung insufficiency on prone positioning

The effect of prone versus supine positioning on lung ventilation and perfusion is controversial

What This Article Tells Us That Is New

In anesthetized and mechanically ventilated healthy volunteers, regional lung ventilation did not differ with position, whereas perfusion was more uniform in the prone position.
In 1978, Rehder et al.\textsuperscript{10} stated that gas distribution, considered an indicator for local ventilation, during general anesthesia and mechanical ventilation, is preferentially dorsal in supine and ventral in the prone position. Thus, that it is dependent at both postures. In contrast with this, Tokics et al.\textsuperscript{14,15} reported, in 1996, that ventilation is predominantly ventral and nondependent in the supine, anesthetized, and mechanically ventilated man. They also reported, in agreement with several other studies,\textsuperscript{12–19} that lung perfusion is predominantly dorsal and dependent in the supine position. Many investigators have found lung perfusion to be more uniform in prone than in supine postures.\textsuperscript{14–21}

Improved blood oxygenation in patients with acute lung insufficiency when turned to prone position has been observed.\textsuperscript{4–8} The underlying mechanisms are still unclear. We hypothesized that the perfusion (Q) distribution along the ventral to dorsal direction in prone posture is less affected by gravity than in supine posture, resulting in a better ventilation (V)/perfusion (Q) matching distribution. Furthermore, it is of interest to study V and Q in humans during general anesthesia and mechanical ventilation to contribute to the discussion of earlier conflicting results. A dual radioisotope technique, previously developed in our group, which enabled simultaneous relative regional measurements of V and Q\textsuperscript{22,23} was used.

Materials and Methods

Subjects

Seven nonsmoking healthy volunteers (mean age, 31 yr; range, 26–39 yr; three men and four women) were included. They were of normal height (mean, 172 cm; range, 163–178 cm) and weight (mean, 70 kg; range, 57–91 kg). The local ethical and radiation safety committees (Stockholm, Sweden) approved the study, and written informed consent was obtained from all participants.

Radiopharmaceuticals

Approximately 50 MBq of [\textsuperscript{99m}Tc]-Technegas (Tetley Manufacturing Ltd., Sydney, Australia) was used as tracer for V. Simultaneously, 50 MBq of [\textsuperscript{113m}In]-labeled macroaggregates of human albumin (TechneScan LyoMAA, Mallinckrodt Medica, Petten, The Netherlands) was used as tracer for Q.

Anesthesia

An intravenous catheter was inserted into a peripheral vein. Monitoring equipment for electrocardiogram and pulse oximetry was applied. During anesthesia, inhaled and exhaled gases were analyzed using a DATEX AS/3 monitoring equipment (Datec Division of Instrumentarium Corp., Helsinki, Finland). Fractions of inhaled oxygen, end-tidal concentrations of carbon dioxide, minute ventilation, respiratory rate, and peripheral arterial oxygen saturation were all recorded. The levels of applied positive end-expiratory pressure were recorded continuously.

Anesthesia was induced by intravenous injection of 200 mg propofol, followed by a continuous infusion of propofol at a rate of 8 mg kg\textsuperscript{-1} h\textsuperscript{-1}. Tracheal intubation was performed after establishing muscle relaxation by intravenous injection of 0.6 mg kg\textsuperscript{-1} rocuronium bromide. Alfentanil was used for analgesia. The subjects were then connected to a Servo 900C ventilator (Siemens-Elema, Stockholm, Sweden) set in a volume-controlled mode. A tidal volume of 8–10 ml/kg, a breathing frequency of 8–12/min, and a positive end-expiratory pressure of 3–4 cm H\textsubscript{2}O were used. Fraction of inhaled oxygen was set at 0.3, and both respiratory rate and tidal volume were continuously adjusted to obtain a constant end-tidal concentration of carbon dioxide. Before administration of the radiopharmaceuticals, an inspiratory recruitment maneuver was sustained for 30 s at an airway pressure of 30 cm H\textsubscript{2}O. The Technegas was then mixed with normal air and inhaled at a constant flow into the endotracheal tube between the Y-piece and the subject.\textsuperscript{24} Simultaneously, the [\textsuperscript{113m}In]-labeled albumin macroaggregates were administered intravenously. After examination, muscle relaxation was reversed, trachea was extubated, and the subject was transferred to the recovery room.

Study Design

The volunteers were fasted for 6 h before examinations. Each subject was examined at two different occasions with single photon emission computed tomography (SPECT) technique (one for isotope administration in prone position and one for isotope administration in supine position), at least 2 days apart and in random order. The study aimed at comparing distribution of radiopharmaceuticals after administration in prone and supine postures, whereas all registrations were performed with the subjects in supine position. Thus, at registration, anatomical conditions are identical. Differences in distribution will therefore be attributed to physiologic conditions at the time of radiopharmaceutical administration.

The study design is shown in figure 1. Induction of anesthesia and muscle relaxation followed by intubation of the trachea was always made in the supine position. When studying V and Q in prone position (fig. 1A), subjects were turned to prone position and a lung recruitment maneuver was performed to minimize atelectasis. Ten minutes after reaching a stable and comfortable prone position, radiopharmaceuticals were simultaneously administered. The subjects were then turned to supine position, and 10 min later, another recruitment maneuver was performed followed by a transmission and a tomography examination.

In part of the investigation, when supine posture was maintained throughout (fig. 1B), recruitment maneuvers were performed 15 min after intubation of the trachea. Ten minutes later, radiopharmaceuticals were administered, and SPECT examinations were performed.

SPECT Examination

A three-headed Triad XLT gamma camera (Trionix, Twinsburg, OH) with medium energy collimators was used. Examinations were performed using a four-energy window SPECT

\textsuperscript{Nyrén et al.}
technique. One primary energy window was centered at 140 keV ($^{99m}$Tc) representing V and another window at 392 keV ($^{113m}$In) representing Q. The remaining two windows were placed just below each of the primary energy windows to allow scatter and spill-down corrections. Acquisition was performed with 72 projections covering 360° and an acquisition time of 25 min. A 128×128-image matrix with a pixel size of 3.56 mm$^2$ was used. A 15-min transmission scan with a $^{99m}$Tc-filled line source was made directly before or after the SPECT study for adequate attenuation correction and to delineate the lungs in the images. Reconstruction was made in the three planes using filtered back projection. Spatial resolution of the reconstructed data, after filter back projection and correction for scatter and attenuation, estimated as the full width half maximum of a point source is 18 mm for $^{99m}$Tc and 25 mm for $^{113m}$In.

**Data Analysis**

After reconstruction and correction for photon scattering, attenuation, activity decay, and organ outline, the SPECT data were pixel-wise normalized to the total activity administered. Thus, each pixel counts represents the relative blood flow or ventilation at that specific position in the lung. The relative ventilation or perfusion distributions were expressed as a percent of the total ventilation or perfusion in each individual.

The lungs of every individual were divided into 21 volumes of interest of equal distance along the ventral to dorsal axis, and the values for V, Q, and ventilation to perfusion (V/Q) ratio were plotted along the ventral to dorsal axis (fig. 2).

To enable intersubject comparison, the coronal projections (3.56-mm thick) were then pixel-wise added into three compartments of equal volume in the anterioposterior direction. The total ventilation, perfusion, and average V/Q ratio in each of these lung compartments were pixel-wise calculated (fig. 3). A two-tailed, paired Student $t$ test with Bonferroni correction was used for significance testing between the three equal volumes (Excel, Microsoft Corporation, Redmond, WA). A $P$ value less than 0.016 was considered statistically significant.

The contribution of the vertical direction to the total heterogeneity of the regional distribution of the ventilation, perfusion, and V/Q ratios, in prone and supine positions, was estimated using a variance analysis of the data set. To ensure that random image noise does not influence the analysis, the root mean square noise component for each SPECT data set was first calculated and then subtracted from the image. Each pixel in the noise-free image was then normalized to the total lung mean pixel value and the total variance ($SS_{total}$) obtained as the sums of squares of the pixel-wise deviations from this mean. In a second step, the mean pixel value for each isogravitational plane was also calculated.
obtained and subtracted from every pixel within that plane. The variance of all these new pixel values for the entire lung was then calculated and considered to represent the residual heterogeneity without the influence from the vertical direction (SS residual). Finally, the variance due to the vertical direction was calculated as the difference between the total and the residual variance.

\[ SS_{vertical} = SS_{total} - SS_{residual} \]  

(1)

The contribution to the total heterogeneity explained by the vertical direction was then obtained as:

\[ SS_{vertical}(\%) = \frac{SS_{vertical}}{SS_{total}} \times 100 \]  

(2)

A two-tailed Student t test was used to compare the SS vertical(%) in prone and supine positions (Excel, Microsoft Corporation). A P value less than 0.05 was considered statistically significant.

**Results**

Recorded routine monitoring variables at the different postures are shown in table 1.

### Table 1. Subjects Vital Parameters at Radiopharmaceutical Administration

<table>
<thead>
<tr>
<th></th>
<th>Supine</th>
<th>Prone</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (per min)</td>
<td>62 ± 12</td>
<td>69 ± 9</td>
<td>0.067</td>
</tr>
<tr>
<td>Fraction of inhaled oxygen (%)</td>
<td>0.31 ± 0.01</td>
<td>0.29 ± 0.02</td>
<td>0.063</td>
</tr>
<tr>
<td>End-tidal oxygen (%)</td>
<td>26 ± 1</td>
<td>25 ± 2</td>
<td>0.269</td>
</tr>
<tr>
<td>End-tidal carbon dioxide (%)</td>
<td>3.9 ± 0.2</td>
<td>3.9 ± 0.2</td>
<td>0.911</td>
</tr>
<tr>
<td>Oxygen saturation of peripheral blood (%)</td>
<td>98 ± 1</td>
<td>98 ± 1</td>
<td>0.457</td>
</tr>
<tr>
<td>Positive-end expiratory pressure (cm H2O)</td>
<td>4 ± 0</td>
<td>5 ± 1</td>
<td>0.200</td>
</tr>
<tr>
<td>Tidal volume (ml)</td>
<td>612 ± 68</td>
<td>594 ± 190</td>
<td>0.743</td>
</tr>
<tr>
<td>Respiratory rate (per min)</td>
<td>10 ± 2</td>
<td>11 ± 4</td>
<td>0.515</td>
</tr>
<tr>
<td>Minute volume (l)</td>
<td>6.1 ± 1.3</td>
<td>6.1 ± 1.3</td>
<td>0.955</td>
</tr>
<tr>
<td>Mean airway pressure (cm H2O)</td>
<td>7.9 ± 2.8</td>
<td>9.4 ± 3.9</td>
<td>0.183</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD.

**Regional Distributions of V, Q, and V/Q**

There were no statistically significant differences in V distribution between prone and supine positions (table 2; figs. 2 and 3). Conversely, the Q distribution differed between prone and supine postures. Table 2 and figures 2 and 3 show a uniform Q distribution over different lung regions in the prone posture, whereas a more dependent distribution in the supine posture.

In ventral and dorsal lung regions, V/Q ratios were different in prone and supine positions, whereas mid-lung portions were similar in both postures (table 2).

**Variance Analysis of the Regional Distribution of V, Q, and V/Q**

The contribution to the total heterogeneity explained by the vertical direction is presented in table 3. The variation of V in the vertical direction (ventral to dorsal) was nearly identical in prone and supine postures (P = 0.589). For Q, however, large variations in the regional distribution along the vertical direction were found between supine and prone postures (P = 0.0006). The fraction of the total variance in the spatial distribution of Q, attributable to the vertical direction, is reduced from 45.8% in supine posture to 20.0% in prone posture (table 3). The fraction of the total variance attributable to the vertical component in the V/Q distribution was reduced from 31.4 ± 14.1% in supine posture to 16.4 ± 14.2% in prone posture (P = 0.0639; table 3). Hence, a

### Table 2. Regional Distribution of Lung Ventilation and Perfusion within the Lung

<table>
<thead>
<tr>
<th></th>
<th>Ventral</th>
<th>Mid</th>
<th>Dorsal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1/3</td>
<td>1/3</td>
<td>1/3</td>
</tr>
<tr>
<td>Ventilation in supine (%)</td>
<td>25 ± 3</td>
<td>34 ± 3</td>
<td>41 ± 2</td>
</tr>
<tr>
<td>Ventilation in prone (%)</td>
<td>24 ± 2</td>
<td>34 ± 2</td>
<td>42 ± 3</td>
</tr>
<tr>
<td>P value</td>
<td>0.28</td>
<td>0.54</td>
<td>0.62</td>
</tr>
<tr>
<td>Perfusion in supine (%)</td>
<td>17 ± 4</td>
<td>34 ± 2</td>
<td>49 ± 4</td>
</tr>
<tr>
<td>Perfusion in prone (%)</td>
<td>31 ± 4</td>
<td>35 ± 3</td>
<td>33 ± 5</td>
</tr>
<tr>
<td>P value</td>
<td>0.0007</td>
<td>0.15</td>
<td>0.0008</td>
</tr>
<tr>
<td>V/Q ratio in supine (%)</td>
<td>1.8 ± 0.5</td>
<td>1.0 ± 0.1</td>
<td>0.8 ± 0.1</td>
</tr>
<tr>
<td>V/Q ratio in prone (%)</td>
<td>0.8 ± 0.2</td>
<td>1.0 ± 0.1</td>
<td>1.4 ± 0.3</td>
</tr>
<tr>
<td>P value</td>
<td>0.003</td>
<td>0.98</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD.

V/Q = ventilation to perfusion ratio.
tendency toward a smaller contribution of the vertical component to the V/Q spatial distribution was observed in prone compared with supine posture.

**Discussion**

The main findings of this study in healthy individuals during anesthesia and mechanical ventilation are as follows:

1. V is not affected by administration posture.
2. Q is dorsally distributed in supine position and is more uniform between different lung regions in prone position.
3. There is a tendency toward a more homogenous V/Q distribution along the vertical direction in prone compared with supine posture.

In contrast to Tokics *et al.*, we found that ventilation seems dependent in supine position in anesthetized mechanically ventilated healthy volunteers. However, Tockcis *et al.* reported the observation of dependent lung atelectasis, which may have been prevented in our study by the use of recruitment maneuvers not described by Tokics *et al.* Another important difference is the quantification of the activity distribution. Although, in our study, we perform a scatter and attenuation correction routine based on transmission scans, Tokics *et al.* report that no correction routines were applied, which results in a false quantification of the activity distribution.

Our results regarding regional distribution of V and Q follow the same pattern as described in previously published investigations in animals (dogs, lambs, baboons, pigs, and sloths) and in humans. In particular, the values reported in the literature for the variation in ventilation explained by positioning in the vertical direction range from 12 to 33% in supine position and from 5 to 25% in prone position. Corresponding values for lung perfusion are between 7 and 73% in supine position and from 5 to 26% in prone position.

The observed lower variation in Q distribution along the vertical direction while in prone position is most likely the main explanation for the improved gas exchange when turned to prone position.

Nuclear medicine techniques are well suited for the study of pulmonary ventilation and blood perfusion. The current technique, developed and evaluated in our group, provides simultaneous relative quantification of V and Q distributions. It also involves individually tailored correction for photon attenuation and scattering, which is necessary for adequate quantification of data in the complex anatomy of the chest. However, SPECT images suffer from a limited spatial resolution that results in partial volume effects, which hampers image quantification in regions near the edge of the object. In our study, we performed edge detection based on anatomical images from the transmission scan. This gives us an accurate definition of the anatomical extensions of the lungs, reducing the impact of partial volume in the calculations of the variance. In fact, the variance calculated in the lungs defined by the edge detection algorithm did not differ from the variance calculated by excluding the most outer 5-pixel thick layer of the lung tissue (data not shown). Another important assumption is that the radiopharmaceuticals are trapped in the alveoli and in the capillary bed in direct proportion to ventilation and perfusion, respectively, and that the activity remains stable throughout the examination. Previous studies have confirmed this. Both tracers are currently used in routine clinical lung scintigraphy.

Based on these results in anesthetized and mechanically ventilated healthy individuals, it is concluded that V is not affected by posture and Q is gravity dependent in supine posture and uniformly distributed between different lung regions in prone posture. From a functional gas exchange standpoint, the tendency for a more evenly distributed V/Q matching along the vertical direction while in prone position, observed in these healthy volunteers, could be more pronounced in patients with acute lung insufficiency.

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**References**