Pulmonary perfusion is more uniform in the prone than in the supine position: scintigraphy in healthy humans

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To further investigate this, lung perfusion scintigraphy was performed in healthy volunteers, using tomographic gamma camera examination [single-photon-emission computed tomography (SPECT)]. Regional pulmonary perfusion was investigated after injection of technetium-99m (99mTc)-labeled macroaggregates of albumin in both prone and supine positions at normal breathing and at lung distension caused by a continuous positive airway pressure (CPAP) of 10 cmH2O. In a supine posture, atelectasis could develop in dorsal parts of the lungs. Using CPAP would minimize that risk and maintain similar lung volumes between supine and prone postures. Transverse tomographic sections representing lung perfusion at the different conditions were achieved and compared. The primary purpose of the investigation was to find out whether the dominant dorsal lung perfusion in supine positions changes to a dominant ventral perfusion when the position becomes prone. We also wanted to examine whether lung distension due to CPAP changed positional variations in lung perfusion.

METHODS
Subjects. Ten healthy volunteers, five men and five women, were included in this investigation. Their mean age was 39 yr (range 24–57 yr). Seven subjects underwent examination at both normal breathing and at a CPAP of 10 cmH2O, one at normal breathing only, and two at CPAP only. The seven subjects, investigated during both CPAP and normal breathing, were examined on two different occasions. The study was approved by the local ethical and radiation protection committees. Written information about the entire procedure was given to all volunteers.

Experimental design. All examinations were performed as illustrated in Fig. 1. With the subject in the prone position on the gamma camera couch, 50 MBq 99mTc-labeled macroaggregates of albumin were injected in the right arm via a vein catheter. Some minutes after the completed injection, the subject turned to the supine position, and a SPECT acquisition of the lungs was made (acquisition 1). This was followed by another injection of 100 MBq of the tracer and an identical SPECT acquisition with the subject in the supine position (acquisition 2).

The volunteers studied during CPAP breathing were also examined 2 wk later during normal breathing. The CPAP of 10 cmH2O was achieved via a modification of an Engström 2000 ventilator (Datex Engström, Solna, Sweden). Air was used, and a tight seal was accomplished by the use of a specialized face mask. Mouth pressures were recorded continuously throughout the CPAP breathing. There was a 10-min equilibration period between application of CPAP breathing and tracer injection. SPECT acquisitions were all made at normal breathing without CPAP, but both injections of the radiotracer were made at CPAP breathing (Fig. 1). From the

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were labeled with 99mTc (TechneScan LyoMAA, Mallinckrodt Medical, Petten, The Netherlands) according to the clinical routine. The manufacturer guarantees that 95% of the particles are between 10 and 100 µm. No particles are larger than 150 µm (largest diameter). The preparation was made so that 50 MBq represented \(1.25 \times 10^6\) particles.

**SPECT examination.** A three-headed Triad XLT gamma camera (Trionix, Twinsburg, OH) with high-resolution, low-energy collimators was used. Each acquisition was performed with subject in supine position. A 128 x 128 matrix with a pixel size of 3.6 x 3.6 mm\(^2\) was used for data acquisition and reconstruction. Each transverse row of the projection matrix was used for reconstruction, thus giving sections with a nominal voxel (volume element) size of 3.6 x 3.6 x 3.6 mm\(^3\).

To match the spatial resolution of the system (\(\sim 15\) mm, full-width half-maximum), a weighing kernel was applied to the actual row for reconstruction was performed, with the two closest consecutive rows on each side before filtering and reconstruction. The weighing kernel was 1, 2, 5, 2, and 1, with a weight of 5 given to the central row. Reconstructions were made respectively, from data obtained during acquisition 1 (representing the perfusion in the prone position) and that obtained by subtracting acquisition 1 data from acquisition 2 (representing the perfusion in the supine position).

**Data analysis.** The activity distribution in the right lung was evaluated at three different levels. Therefore, the lateral two-dimensional reprojected image of the right lung was first divided into five segments of equal height from the top to the base, where the last segment was omitted. At each of the three borderlines between the remaining four segments, three consecutive 3.6-mm-thick transverse sections were added, thus giving three – 10-mm-thick sections. The location of the section closest to the upper part of the lung was denoted “apical,” the next “intermediate,” and the third, closest to the base, “diaphragmatic.” In no subject did the diaphragm interfere with the diaphragmatic section.

The activity distribution along the ventral-dorsal direction of these three selected transverse sections of the right lung was assessed by plotting activity profiles of a 40-mm-wide row of voxel data at the center of each section (Fig. 2). Each curve was subsequently “divided” into three equal parts, with average data in each part representing the activity (in percentage of the total in the actual 40-mm row) in the ventral, mid-, and dorsal region of the section.

Nuclear medicine images suffer from low spatial resolution and disturbing influence from attenuation and contribution of unwanted scattered photons. Therefore, an accurate (mm) definition of an organ outline may often be difficult to make. In this investigation, we made use of an approximative method, whereby we defined the outline as the intersection between the mean of the data in the 128-voxel-long profile and the actual activity profile. These defined border outlines agreed with those from visual inspection.

By using this method, identical lung portions were assessed in each individual at the two registrations. This allowed comparison of regional perfusion at two different postural positions. Nine examinations comparing the prone and supine positions at CPAP and eight similar examinations at normal breathing were performed. Similar analyses were made comparing CPAP with normal breathing.

**Statistics.** Mean and SD values of regional activities across subjects were calculated. Comparisons between the percent activity of the same portion of the slice were made by the standard double-tailed paired and unpaired t-test. \(P < 0.05\) was considered statistically significant.

**RESULTS**

A representative example of activity profiles in the gravitational plane for both lungs together from one individual during normal breathing and CPAP is shown in Fig. 3. At CPAP breathing, the distribution of perfusion was more uniform in the prone than in the supine position (Figs. 3 and 4). The corresponding

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**Diagram**: A schematic presentation of study sequence for single-photon-emission computed tomography (SPECT) assessment of pulmonary perfusion distribution in prone and supine positions using iv injections of \(\text{99mTc}^{-}\)-labeled albumin macroaggregates (administrations (Adm) 1 and 2). At each examination (SPECT 1 and 2), both injections of radiotracer were made at either normal breathing or continuous positive airway pressure (CPAP).
profiles obtained at normal breathing are similar but less pronounced (Fig. 3).

The following data analysis was done on the slices made in the three transverse sections (apical, intermediate, and diaphragmatic) of the right lung (Fig. 2). From each of these slices, the activity in the ventral-dorsal direction (gravitational plane) was evaluated.

Lung perfusion in the prone and supine positions. During normal breathing, there were no differences between prone and supine positions in mid-, dependent, or nondependent vertical regions of apical and intermediate sections of the lung. In the diaphragmatic section, dependent regions were better perfused in the supine than in the prone position. The opposite was observed for nondependent regions, indicating a more uniformly distributed lung perfusion in diaphragmatic sections of the lung while the subjects were in the prone position (Fig. 5).

During CPAP breathing, as during normal breathing, there were no differences between prone and supine positions in the apical and the intermediate sections of the lung (Fig. 5). In the diaphragmatic section of the lung, perfusion was greater in dependent regions while the subjects were in the supine position (P < 0.01, Fig. 6).

During CPAP breathing in the prone posture, lung perfusion was more uniformly distributed during normal breathing than during CPAP. In the apical section of the lung, the perfusion was similar during CPAP and normal breathing in dependent and nondependent regions. Intermediate and diaphragmatic sections of the lung had, during CPAP, a greater perfusion in dependent regions (P < 0.01, Fig. 6). Hence lung perfusion was more uniform during normal breathing in the prone position.

Normal breathing vs. CPAP in the supine posture. In the supine position, the CPAP effect on gravitational blood flow dependence was more pronounced, particularly in the diaphragmatic section of the lung, compared with normal breathing (P < 0.001, Fig. 6). During CPAP breathing, perfusion of the diaphragmatic section of the lung decreased from 49 ± 7% in dependent to 16 ± 4% in nondependent regions (Fig. 6). Corresponding values during normal breathing only decreased from 38 ± 3 to 25 ± 3%.

DISCUSSION

The main finding in this study was that the dominant dorsal lung perfusion in the supine position did not change into a dominant ventral perfusion in the prone position. Lung perfusion was more uniformly distributed in the prone compared with the supine position. CPAP breathing enhanced perfusion differences along the gravitational axis, a result that was more pronounced in the supine than in the prone position.

Methodological issues. Perfusion scintigraphy of the lung (SPECT) is accomplished by microembolization of radionuclide-labeled particles in the arterial pulmonary circulation. It is based on the concept that the number of particles that are trapped in a particular lung volume is proportional to the pulmonary arterial blood flow to that region (16, 26). Studies comparing the distribution of N,N',N'-trimethyl-N-[2-hydroxy-3-methyl-5-iodobenzyl]-1,3-propanediamine, a diamine with a near-complete first-pass extraction by the lungs, have shown that the principle used in the present study reflects regional pulmonary blood flow (17). SPECT is now an established technique for tomographic investigations of radiotracer distribution, allowing reconstruc-
tion of sectional images in any plane. Several previous investigations on the present topic have also been based on this technique (10, 14, 22, 25).

The subtraction technique used in the present study was appropriate because the removal of albumin macroaggregates of the actual size is very slow (24). However, increased image noise affects our subtracted data. This unwanted effect was reduced by injecting twice as much radiotracer before acquisition 2. Another problem, photon scattering, may explain why a higher activity was measured in midlung regions compared with independent and nondependent regions, in the apical and intermediate sections of the lung (Figs. 5 and 6). Yet another explanation is that perfusion is higher in midregions of the lung, which are closer to the hilus. Walther et al. (27) found that the blood flow was larger in hilar than in peripheral regions in awake prone sheep.

The present study was designed to answer whether the pattern for perfusion varies between prone and supine postures. The experimental design, including assessment of the same individual at the two occasions, is considered adequate to reduce biological variations and to allow evaluation of results by using paired comparisons of perfusion at different postural positions (Fig. 5). Evaluations of CPAP influence (Fig. 6) could, however, only be carried out by unpaired comparisons.

Anatomic considerations. To assess the perfusion, the right lung was chosen to avoid interference with the heart. Comparing the perfusion in prone and supine positions, there was no difference in the apical and intermediate sections (Fig. 5), and there was no effect of CPAP in the apical section (Fig. 6), whereas differences occurred in the diaphragmatic sections. A similar discrepancy between various levels of the lung has also been reported previously (13). It may be explained by

![Diagram](http://jap.physiology.org/Downloaded-from)
the fact that, for anatomic reasons, upper ventral-dorsal slices are too short for gravitational influences to be expressed, compared with slices from diaphragmatic sections of the lung with a longer distance in the gravitational plane.

The evaluation of the three lung sections was based on small-volume units of identical size and shape, without consideration for the total perfusion or configuration of the lung. This allowed the direct comparison of activity between different pulmonary regions, i.e., ventral vs. dorsal portions of the lung. When the net effect of all lung sections is given, it must be governed by the characteristics of the diaphragmatic lung sections, because they strongly dominate quantitatively.

Distribution of lung perfusion. It is known that lung volumes increase at a CPAP of 10 cmH₂O. It is also known that large lung volumes, above functional residual capacity, are related to increased vascular resistance of small vessels, creating zone 1 and zone 2 conditions in nondependent regions (12, 28). The West model of blood flow distribution within the lung, which is based on gravity (28), can no longer act as the only explanatory model for lung perfusion. In contrast, several reports from experiments in various quadruped animals, in baboons as well as in upright humans, have indicated that gravity is a minor rather than a major determinant of regional pulmonary blood flow. Instead, intrinsic factors, possibly regional differences in vascular conductance, may be of importance (2, 4, 7–11, 20, 22, 29). These opinions are also supported by results in the present study. The blood flow to dependent lung regions, particularly in the diaphragmatic sections of

Fig. 6. Analysis of effect of CPAP on distribution of lung perfusion in right lung while subject was in prone (left) or supine position (right). Mean percent activity of identical slice portion was compared between CPAP and normal breathing at 3 different lung levels. For statistical analysis, standard double-tailed unpaired t-test was used: *0.01 ≤ P < 0.05, **0.001 ≤ P < 0.01, ***P < 0.001.
the lungs, was, during normal breathing, relatively greater in the supine than in the prone position. The more uniformly distributed perfusion between dependent and nondependent regions in the prone position is in accordance with gravity being only of minor importance for determination of regional lung perfusion (7).

The well-maintained perfusion in nondependent lung regions in the prone position supports the finding of Beck and Rehder (4), who, in an in vitro study of dog lungs, found that there were regions with higher vascular conductance. These regions were always located dorsocaudally. This is purposeful in dogs, which walk on four legs, where gravity acts on blood flow in one direction, to be offset by higher vascular conductance dorsocaudally to achieve an even lung perfusion.

In the present series, the prone position clearly resulted in a more even lung perfusion, which is in conformity with the reasoning above on the basis of Beck and Rehder’s findings in dogs. The question is whether regional variation in resistance to blood flow exists also in upright humans. In light of evolution, such similarities between species are not surprising, and certainly these matters must be further elucidated in future studies.

At CPAP, lung volumes increase. In the supine position, blood flow is enhanced to dependent parts of the lung in the diaphragmatic section. An explanation for this could be increased lung regions in zone 1 and zone 2 conditions in nondependent regions (28). This means more blood to dorsal regions while in the supine position. Higher vascular conductance in the dorsocaudal regions, independent of posture, is probably the reason the effect of gravity dependence on blood flow distribution was more pronounced in the supine than in the prone position during CPAP breathing compared with normal breathing. Still, however, lung perfusion was more homogeneous in the prone than the supine position (Figs. 5 and 6). From a clinical point of view, this is of interest for patients suffering from lung insufficiency demanding mechanical ventilation. The prime clinical goal for these patients is to reach the best match of ventilation and perfusion to get an optimal gas exchange. A major complication is that, in anesthetized, mechanically ventilated patients, distribution of inspired gas to nondependent lung regions is greater (25). At the same time, as shown in this study, positive airway pressures result in a higher blood flow to dependent regions, particularly when in the supine position. The summation of these effects reinforces a ventilation-perfusion mismatch in the supine position.

In the prone position, however, the more uniformly distributed lung perfusion, also during positive airway pressures, offers conditions for better matching, with the resultant improved gas exchange.

It was concluded that pulmonary blood flow distribution during normal breathing was more uniform in the prone than in the supine position. The combination of gravity and other factors, such as vascular anatomy, results in a greater vertical gradient of perfusion in the supine compared with in the prone posture. Positive pressure breathing at a CPAP of 10 cmH₂O resulted in a more marked gravity dependence on blood flow in the supine position and now also, but to a much lesser degree, while in the prone position. Because the distribution of inspired gas at positive airway pressure preferably goes to nondependent lung regions, ventilation-perfusion matching during positive pressure breathing is most probably less favorable in the supine than in the prone position.

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