Effects of positive end-expiratory pressure on anesthesia-induced atelectasis and gas exchange in anesthetized and mechanically ventilated sheep

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Objective—To evaluate the effects of 10 cm H₂O of positive end-expiratory pressure (PEEP) on lung aeration and gas exchange in mechanically ventilated sheep during general anesthesia induced and maintained with propofol.

Animals—10 healthy adult Bergamasca sheep.

Procedures—Sheep were sedated with diazepam (0.4 mg/kg, IV). Anesthesia was induced with propofol (5 mg/kg, IV) and maintained with propofol via constant rate infusion (0.4 mg/kg/min). Muscular paralysis was induced by administration of vecuronium (25 µg/kg, bolus IV) to facilitate mechanical ventilation. After intubation, sheep were positioned in right lateral recumbency and mechanically ventilated with pure oxygen and zero end-expiratory pressure (ZEEP). After 60 minutes, 10 cm H₂O of PEEP was applied for 20 minutes. Spiral computed tomography of the thorax was performed, and data were recorded for hemodynamic and gas exchange variables and indicators of respiratory mechanics after 15 (T₁₅), 30 (T₃₀), and 60 (T₆₀) minutes of ZEEP and after 20 minutes of PEEP (Tₑₑₑₑ),. Computed tomography images were analyzed to determine the extent of atelectasis before and after PEEP application.

Results—At Tₑₑₑₑ, the volume of poorly aerated and atelectatic compartments was significantly smaller than at T₁₅, T₃₀, and T₆₀, which indicated that there was PEEP-induced alveolar recruitment and clearance of anesthesia-induced atelectasis. Arterial oxygenation and static respiratory system compliance were significantly improved by use of PEEP.

Conclusions and Clinical Relevance—Pulmonary atelectasis can develop in anesthetized and mechanically ventilated sheep breathing pure oxygen; application of 10 cm H₂O of PEEP significantly improved lung aeration and gas exchange. (Am J Vet Res 2010;71:867–874)
of the alveolar gas (absorption atelectasis) are the main pathogenic mechanisms leading to pulmonary atelectasis during general anesthesia. A high FiO2 promotes the development of absorption atelectasis by increasing the rate and amount of gas absorbed into pulmonary capillary blood. Atelectasis has been proposed as the major cause of impaired pulmonary gas exchange and decreased lung compliance in anesthetized human patients independent of the anesthetic protocol and technique used. Therefore, increasing FiO2 during general anesthesia may improve anesthetic safety only at the cost of aggravating 1 mechanism responsible for gas exchange derangement.

The application of PEEP aimed at reopening (ie, recruiting) collapsed alveolar units has been proposed to treat anesthesia-induced atelectasis. Several studies in human patients revealed that low values of PEEP (5 to 10 cm H2O) are effective in reducing lung atelectasis during anesthesia. The effects of PEEP on gas exchange are more controversial; investigators in some studies reported improved gas exchange, and others failed to identify this effect or even detected reduced arterial oxygenation. The inconsistency with which PEEP affects gas exchange in humans and nonhuman animals has been associated with the impact PEEP may have on pulmonary and systemic blood circulation.

Sheep are often anesthetized in clinical and research environments. Information regarding the effects of anesthesia on lung function in sheep is limited, although these animals have been used in a study to investigate physiologic and pathophysiologic characteristics of human lungs. Computed tomography is the preferred technique used.

Materials and Methods

Animals—Ten healthy female Bergamasca sheep from a research herd at the University of Bari (mean ± SD weight, 56 ± 9 kg [range, 45 to 68 kg]; mean ± SD age, 17 ± 2 months [range, 14 to 22 months]) were included in the study. The sheep were housed and all experiments were conducted at the School of Veterinary Medicine at Bari. During the experimental period, the sheep were housed together in 1 indoor stall (size, approx 40 m2). The diet consisted of grass and hay, and the sheep had free access to water; they were acclimated to these conditions for 1 month prior to the start of the study. Food was withheld for 24 hours before anesthetic induction. The sheep were considered healthy on the basis of the results of physical examination, which included hematologic, arterial blood gas, and serum biochemical analyses. The study protocol was approved by the Italian Ethical Committee of the Ministry of Health, Bari.

Anesthetic protocol and monitoring—All anesthetic inductions were performed in the CT suite. Skin at the site of venipuncture was surgically prepared and infiltrated with 1 mL of a 2% solution of lidocaine hydrochloride and a 14-gauge catheter was placed in a jugular vein of each sheep. Midazolam hydrochloride (0.4 mg/kg, IV) was administered for sedation. After 5 minutes, anesthesia was induced with propofol (5 mg/kg, IV), and tracheal intubation was accomplished by use of a cuffed endotracheal tube (inner diameter, 12 mm). Sheep were positioned in sternal recumbency for intubation and subsequently moved into right lateral recumbency for the remainder of the study. Anesthesia was maintained by use of a constant rate infusion of propofol (0.4 mg/kg/min), and lactated Ringer’s solution was infused at a rate of 10 mL/kg/h during the entire anesthetic procedure. Muscle paralysis was induced by administration of vecuronium (25 μg/kg, bolus IV) to facilitate mechanical ventilation and to avoid any interference of chest wall muscle tone on lung mechanics measurements.

The median auricular artery of the left pinna was percutaneously catheterized by use of a 20-gauge catheter to record arterial blood pressures (systolic, diastolic, and MAP) and to facilitate collection of arterial blood samples. Hemoglobin oxygen saturation (via pulse oximetry), PET CO2 (via a capnometer), heart rate (via ECG), and rectal temperature (via a digital thermometer) were continuously recorded.

Neuromuscular function was monitored with a peripheral nerve stimulator operating in the train-of-4 stimulation mode. Complete neuromuscular blockade (absence of any twitch response during train-of-4 nerve stimulation) was confirmed before the respiratory maneuvers were performed; on completion of the experiment after edrophonium and atropine administration, 4 responses (switches) to train-of-4 nerve stimulations were required before the constant rate infusion of propofol was discontinued and sheep were allowed to recover from anesthesia with appropriate monitoring and assistance.

Mechanical ventilation and experimental protocol—Immediately after intubation, sheep were connected to a nonrebreathing circuit and mechanically ventilated by use of a respirator operated in a volume-controlled, time-cycled mode with a constant fresh gas flow, FiO2 of 1 (ie, 100% oxygen). Vt of 12 mL/kg, and inspiratory-to-expiratory ratio of 1:3 with ZEEP. The respiratory rate was adjusted to maintain PET CO2, at 35 to 45 mm Hg. The FiO2 (maintained at 1) was continuously monitored during the experiment by use of an oxygen sensor located inside the ventilator.
Sheep were positioned in right lateral recumbency; this was considered time 0 (ie, T$_0$). Spiral CT scan of the thorax was performed at 15, 30, and 60 minutes with ZEEP (ie, T$_{15}$, T$_{30}$, and T$_{60}$, respectively), and arterial blood gas analysis was performed from samples obtained at each time point. Sixty minutes later positioning the sheep in right lateral recumbency, 10 cm H$_2$O of PEEP was applied for 20 minutes, without changing the ventilatory pattern settings. The CT and blood gas analysis were repeated after PEEP was applied for 20 minutes (ie, T$_{60}$).

Evaluation of respiratory system mechanics—
Measurement of respiratory system mechanics was performed at T$_{15}$, T$_{30}$, T$_{60}$, and T$_{60}$ according to the following methods. Flow was measured with a heated pneumotachograph, which was connected to a differential pressure transducer inserted between the Y-piece of the ventilator circuit and the endotracheal tube. The response to the pneumotachograph was linear over the experimental range of gas flows. The transducer was calibrated before each experiment via a 1-point calibration procedure. Volume was determined via numerical integration of the flow signal. The Pao was measured proximal to the endotracheal tube by use of a pressure transducer. All variables for respiratory system mechanics were displayed and collected on a personal computer and a 12-bit analogue-to-digital converter board at a sampling rate of 200 Hz. The difference between the PEEP set on the ventilator (ie, the Pao value at the end of a regular breath [PEEP$_{set}$/Pao]), and the pressure in Pao during a 3- to 5-second end-expiratory pause (ie, PEEP$_{end}$/Pao) was measured, and this value was regarded as the static intrinsic PEEP (ie, PEEP$_{static}$). The end-expiratory pause was performed by use of the expiratory hold on the ventilator. The CSTAT was calculated at T$_{15}$, T$_{30}$, T$_{60}$, and T$_{60}$ as: CSTAT = V/Plat, where Plat is the Airway plateau pressure corresponding to the value of Pao after an end-inspiratory pause of 3 to 4 seconds. PEEP$_{end}$/Pao = PEEP (applied by the ventilator) corresponding to the value of the Pao at the end of a regular breath. PEEP$_{end}$ = PEEP value that takes into account the possible intrinsic PEEP and corresponds to the value of the Pao at the end of an end-expiratory pause of 3 to 4 seconds.

Collection and analysis of CT images—Frontal topograms and helical CT images of the thorax were obtained by use of a third-generation spiral CT scanner. The CT images were acquired at a setting of 120 kVp and 160 mA (1 second • time) by use of a lung window opening pressure (bottom) obtained from a representative healthy adult sheep mechanically ventilated with pure oxygen during anesthesia induced and maintained with propofol (5 mg/kg and 0.4 mg/kg/min; respectively, IV; muscular paralysis was induced via bolus administration of vecuronium [25 µg/kg, IV]). Tracings indicate the end-inspiratory and end-expiratory pauses separated by a regular breath (ie, without an occlusive pause). Pao$_{plat}$ = Airway plateau pressure corresponding to the value of Pao after an end-inspiratory pause of 3 to 4 seconds.

The right and left lungs were chosen as ROIs for analysis; portions of the pulmonary hila containing the trachea, main bronchi, and hilar blood vessels were excluded from the ROIs. Distributions of radiographic attenuations (expressed in HUs) among the selected ROIs were plotted by use of the computer software. In accordance with a previous study in dogs, the following regions or compartments were identified within the lungs: hyperinflated (ie, composed of pixels with CT numbers of −1,000 to −901 HUs), normally aerated (ie, composed of pixels from −900 to −501 HUs), poorly aerated (ie, composed of pixels with CT numbers of −500 to −101 HUs), and nonaerated (ie, atelectatic; composed of pixels with CT numbers of −100 to 100 HUs).

The gas volume of each ROI (ie, ROI$_{gas}$) was computed by including pixels with density values of −1,000 to 100 HUs according to the following formula: gas volume (mL) = CT number/(−1,000) • voxel volume, where each voxel is a pixel (ie, parallelogram with a square base (0.59 mm/side)) and a height corresponding to the CT slice thickness (10 mm); this was calculated as the area of the pixel times the CT slice thickness. The volume of each compartment (ie, hyperinflated, normally aerated, poorly aerated, and atelectatic) within the ROI was calculated by use of the same formula.

The EELV for each sheep was calculated as the sum of all ROI$_{gas}$ for all CT images obtained, and the total volume of each lung compartment was calculated as the sum of all volumes for a specified compartment in all CT slices. The total volume of each compartment was expressed as a percentage of the EELV.

The PEEP-induced alveolar recruitment was calculated as the difference in the volume of the atelectatic lung
Table 1—Mean ± SD hemodynamic and respiratory values in 10 healthy adult sheep mechanically ventilated with pure oxygen during anesthesia induced and maintained with propofol (5 mg/kg) and 0.4 mg/kg/min, respectively, IV; muscular paralysis was induced via bolus administration of vecuronium (25 μg/kg, IV).

<table>
<thead>
<tr>
<th>Variable</th>
<th>T₁₅</th>
<th>T₆₀</th>
<th>T₁₅₀</th>
<th>T₁₅₀₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>108 ± 8</td>
<td>108 ± 11</td>
<td>113 ± 17.4</td>
<td>111 ± 18</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>109 ± 11</td>
<td>110 ± 9</td>
<td>111 ± 17</td>
<td>108 ± 11</td>
</tr>
<tr>
<td>RR (breaths/min)</td>
<td>9 ± 2</td>
<td>9 ± 2</td>
<td>9 ± 2</td>
<td>9 ± 2</td>
</tr>
<tr>
<td>PtcO₂ (mm Hg)</td>
<td>35.6 ± 3.2</td>
<td>36.3 ± 2.5</td>
<td>36.2 ± 5.0</td>
<td>37.0 ± 5.3</td>
</tr>
<tr>
<td>SpO₂ (%)</td>
<td>99.8 ± 0.1</td>
<td>99.2 ± 5.3</td>
<td>99.1 ± 1.1</td>
<td>99.3 ± 0.7</td>
</tr>
</tbody>
</table>

Sheep were positioned in right lateral recumbency (time of positioning = time 0). Data were recorded at predetermined intervals (15 minutes [T₁₅], 30 minutes [T₆₀] and 60 minutes [T₁₅₀] with ZEEP and after application of 10 cm H₂O of PEEP for 20 minutes [T₁₅₀₀]). HR = Heart rate. RR = Respiratory rate. SpO₂ = Oxygen saturation as measured via pulse oximetry.

Blood gas measurements—Blood gas measurements and related analyses were performed by use of an automated arterial blood gas analyzer. The analyzer was calibrated each day and prior to each experiment. Arterial blood samples were collected anaerobically at T₁₅, T₆₀, T₁₅₀, and T₁₅₀₀ before CT images were obtained; samples were analyzed immediately. The pH of arterial blood, Pao₂, and Paco₂ were measured. All arterial blood gas values were corrected within the analyzer for body temperature of the sheep (measured per rectum at the time of sampling). The PAO₂-Paco₂ was calculated for each sheep, according to the alveolar gas equation:

\[ \text{PAO}_₂ - \text{Paco}_₂ = (\bar{P}_\text{b} - \text{P}_{100\%}) \times \text{FiO}_₂ - \text{Paco}_₂ - \text{Paco}_₂ \]

where \( \bar{P}_\text{b} \) is the barometric pressure and \( P_{100\%} \) is the water vapor pressure. The \( \bar{P}_\text{b} \) was recorded by the arterial blood gas analyzer during each analysis, and the \( P_{100\%} \) was corrected for the rectal temperature of the sheep recorded at the time of arterial blood collection. The V̇O₂ was estimated as a percentage of V̇t by use of the following equation:

\[ \text{V̇O}_₂/V̇t = (\text{Paco}_₂ - \text{PetcO}_₂)/\text{Paco}_₂ \times 100 \]

where PetcO₂ is the value measured at the moment of arterial blood collection.

Statistical analysis—The mean ± SD was determined for each numeric variable. Normal distribution of data was verified by use of a Shapiro-Wilk test. Variables for lung function, lung aeration, and cardiovascular function obtained at T₁₅, T₆₀, T₁₅₀, and T₁₅₀₀ were compared among time points. Statistical analysis included a 1-way ANOVA for repeated measures followed by Student-Newman-Keuls test. Values of P < 0.05 were considered significant.

Results

Experimental procedures were completed in all sheep without complications. Mean ± SD scanning time per helical CT was 65 ± 5 seconds. No patho-

Figure 2—Relative sizes of 4 functional lung compartments identified via analysis of CT images obtained from 10 propofol-anesthetized sheep positioned in right lateral recumbency (time of positioning = time 0). Bars represent mean ± SD percentage of the EELV. Data were recorded at predetermined intervals (15 minutes [T₁₅], 30 minutes [T₆₀] and 60 minutes [T₁₅₀] with ZEEP and after application of 10 cm H₂O of PEEP for 20 minutes [T₁₅₀₀]). Within each anatomic compartment, values with different letters are significantly (P < 0.05) different among time points on the basis of a 1-way ANOVA for repeated measures and a Student-Newman-Keuls test. See Figure 1 for remainder of key.

Figure 3—Distribution of atelectasis throughout the lungs in 10 propofol-anesthetized sheep. One voxel is a pixel (ie, parallelogram with a square base [0.69 mm/side]) and a height corresponding to the CT slice thickness (10 mm); bars represent the mean number of voxels with an HU value between –100 and 100 (ie, the HU range indicative of atelectasis). Transverse CT slices were equally distributed across the entire lung; CT slice numbers represent images obtained serially as the scan proceeded in a cranial to caudal direction (slices with low numbers were obtained from the most cranial lung fields, and slices with high numbers were obtained from the most caudal lung fields). Data were recorded at T₆₀ with ZEEP (white bars) and at T₁₅₀₀ (black bars). See Figures 1 and 2 for remainder of key.
logically altered lung parenchyma was detected in any sheep during preliminary examination of CT images; thus, no sheep were excluded from the study.

Heart rate, MAP, respiratory rate, $\text{PETCO}_2$, and hemoglobin oxygen saturation measured during mechanical ventilation at $T_{15}$, $T_{30}$, $T_{60}$, and $T_{\text{PEEP}}$, did not differ significantly among time points (Table 1). The EELV was significantly greater at $T_{\text{PEEP}}$ (3.0 ± 0.4 L), compared with values recorded at $T_{15}$ (2.1 ± 0.3 L), $T_{30}$ (2.2 ± 0.5 L), or $T_{60}$ (2.2 ± 0.6 L). The relative sizes of lung compartments (ie, hyperinflated, normally aerated, poorly aerated, and atelectatic) were determined for the various experimental conditions (Figure 2). The volume of the normally aerated compartment represented a significantly greater percentage and the poorly aerated and atelectatic compartments represented a significantly lesser percentage of the EELV at $T_{\text{PEEP}}$ compared with the volumes at ZEEP (ie, $T_{15}$, $T_{30}$, and $T_{60}$). Notably, the volume of the hyperinflated compartment did not change among the different experimental conditions.

When both lungs were considered together as an ROI, the volume of the atelectatic compartment (ie, atelectatic lung) was decreased by 5.8 ± 3.2%, compared with the value at $T_{60}$. When each individual lung was considered as an ROI, the volume of the atelectatic compartment was significantly ($P = 0.01$) decreased by 33.8 ± 6.3% in the right (ie, dependent) lung (from 0.143 ± 0.002 L at $T_{15}$ to 0.095 ± 0.009 L at $T_{\text{PEEP}}$) and by 6.62 ± 2.32% in the left lung (from 0.045 ± 0.003 L at $T_{60}$ to 0.042 ± 0.004 L at $T_{\text{PEEP}}$). The distribution of atelectatic lung tissue (detected as voxels with an HU value between –100 and 100) across the entire length of both lungs in a craniocaudal direction revealed increased atelectasis formation in the caudal (slices 12 through 26) lung fields (Figure 3).

Transverse CT images of the thorax (at the level of the body of T8) were obtained (Figure 4). Atelectasis of the parenchyma in the dependent lung was detectable in the CT images obtained at $T_{15}$, $T_{30}$, and $T_{60}$ at $T_{\text{PEEP}}$, the amount of atelectasis is reduced (white arrow). See Figure 2 for remainder of key.

Table 2—Mean ± SD values for pulmonary gas exchange and respiratory dead space variables in 10 propofol-anesthetized sheep during mechanical ventilation.

<table>
<thead>
<tr>
<th>Variable</th>
<th>$T_{15}$</th>
<th>$T_{30}$</th>
<th>$T_{60}$</th>
<th>$T_{\text{PEEP}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{Pao}_2$ (mm Hg)</td>
<td>417 ± 90a</td>
<td>426 ± 77a</td>
<td>416 ± 67a</td>
<td>566 ± 78a</td>
</tr>
<tr>
<td>$\text{Paco}_2$-$\text{Pao}_2$ (mm Hg)</td>
<td>230 ± 57a</td>
<td>228 ± 46a</td>
<td>237 ± 49a</td>
<td>61 ± 8a</td>
</tr>
<tr>
<td>$\text{PaCl}$ (mm Hg)</td>
<td>42.0 ± 3.2a</td>
<td>40.1 ± 3.1a</td>
<td>39.1 ± 4.3a</td>
<td>38.3 ± 3.5a</td>
</tr>
<tr>
<td>$\text{Vcl/VR}$ (%)</td>
<td>8.52 ± 2.31a</td>
<td>9.20 ± 3.11a</td>
<td>7.96 ± 3.21a</td>
<td>8.31 ± 2.21a</td>
</tr>
</tbody>
</table>

± Within a row, values with different superscript letters are significantly ($P < 0.05$) different among time points as determined on the basis of a 1-way ANOVA for repeated measures and a Student-Newman-Keuls test.

See Table 1 for remainder of key.

Table 3—Mean ± SD values for indicators of respiratory system mechanics in 10 propofol-anesthetized sheep during mechanical ventilation.

<table>
<thead>
<tr>
<th>Variable</th>
<th>$T_{15}$</th>
<th>$T_{30}$</th>
<th>$T_{60}$</th>
<th>$T_{\text{PEEP}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{Pao}_{\text{peak}}$ (cm H$_2$O)</td>
<td>17.0 ± 4.2a</td>
<td>16.9 ± 3.6a</td>
<td>17.2 ± 4.0a</td>
<td>26.0 ± 4.0a</td>
</tr>
<tr>
<td>$\text{Pao}_{\text{plat}}$ (cm H$_2$O)</td>
<td>13.9 ± 3.1a</td>
<td>14.6 ± 3.9a</td>
<td>14.4 ± 3.2a</td>
<td>20.0 ± 4.0</td>
</tr>
<tr>
<td>PEEP$_{\text{in}}$ (cm H$_2$O)</td>
<td>0.22 ± 0.02a</td>
<td>0.09 ± 0.03a</td>
<td>0.13 ± 0.05a</td>
<td>10.1 ± 0.20b</td>
</tr>
<tr>
<td>PEEP$_{\text{res}}$ (cm H$_2$O)</td>
<td>0.22 ± 0.02a</td>
<td>0.09 ± 0.03a</td>
<td>0.13 ± 0.05a</td>
<td>0.11 ± 0.02a</td>
</tr>
<tr>
<td>CSTAT$_{\text{alv}}$ (ml/cm H$_2$O)</td>
<td>40.6 ± 3.3a</td>
<td>40.4 ± 2.5a</td>
<td>40.2 ± 4.4a</td>
<td>55.1 ± 2.8a</td>
</tr>
</tbody>
</table>

$\text{Pao}_{\text{peak}}$ = Peak airway opening pressure. $\text{Pao}_{\text{plat}}$ = Inspiratory plateau airway opening pressure. PEEP$_{\text{in}}$ = Intrinsic positive end-expiratory pressure. PEEP$_{\text{res}}$ = Total positive end-expiratory pressure.

See Tables 1 and 2 for remainder of key.
ues at \( T_{15}, T_{30}, \) and \( T_{60} \) (Table 2). Because pure oxygen was used for ventilation throughout the experiment (ie, the \( \text{FiO}_2 \) remained constant at 1), the effects of PEEP on the \( \text{PaO}_2 - \text{FiO}_2 \) ratio were identical to those on \( \text{PaO}_2 \). The \( \text{CSTAT} \) was significantly increased at \( T_{\text{PEEP}} \) compared with values calculated at \( T_{15}, T_{30}, \) and \( T_{60} \) (Table 3).

Statistical analysis was performed for the remaining data (rectal temperature, pH, \( \text{PaCO}_2 \), and \( V_{DSS} \)) obtained during the experiments. Results of this analysis did not indicate any significant differences among time points.

**Discussion**

Results of the study reported here supported our hypothesis that mechanical ventilation with pure oxygen in propofol-anesthetized sheep would result in lung atelectasis, impaired pulmonary mechanics, and reduced gas exchange and that application of 10 cm H\(_2\)O of PEEP would substantially improve these functions by reopening small airways and recruiting previously collapsed alveoli. Even in healthy sheep, poorly aerated and atelectatic lung compartments begin to form rapidly during anesthesia when animals are mechanically ventilated and inspire pure oxygen.\(^{28}\) Our data indicate that the change in lung aeration in sheep is not necessarily the result of a slowly progressive process but develops quickly and may then remain fairly static throughout the anesthetic procedure (Figures 2 and 4). This observation is consistent with the results of a study\(^{21}\) in anesthetized humans ventilated with pure oxygen, in which pulmonary atelectasis was detected within the first 5 to 10 minutes of anesthesia but did not increase with advancing time. The results of the present study revealed that the percentages of poorly aerated and atelectactic lung parenchyma detected during the initial anesthetic period (ie, \( T_{15} \)) were approximately 30% and 7%, respectively, indicating that nearly 40% of the lung tissue was not properly aerated. Atelectases were predominant in the more caudal lung fields (ie, slices 12 through 26), close to the diaphragm, where the main abdominal compression forces are localized.

In sheep and in ruminants in general, the compression exerted by the rumen can substantially impair lung function during anesthesia, compared with the lung function of anesthetized monogastric animals.\(^{27}\) Indeed, the rumen frequently remains filled with content, even after feed is withheld for an extended period prior to anesthesia. Fermentation also continues during general anesthesia and eructation usually ceases, which promotes tympanic expansion of the rumen and further impairment of lung inflation during inspiration.\(^{27,28}\) We determined that atelectases were more pronounced in the dependent lung of sheep in lateral recumbency (Figure 4). This finding was similar to the results of a study\(^{29}\) in anesthetized, mechanically ventilated human patients in lateral recumbency, which indicated that the dependent lung, although better perfused, is subject to more widespread small-airway closure and atelectasis formation and thus to increased \( V_{Q}/V_{T} \) mismatching. Furthermore, the \( V_{T} \) distributes preferentially in the nondependent lung; this increases the risks of alveolar hyperinflation and further impairment of gas exchange (caused by increased dead space) and may result in lung injury.\(^{29}\)

The principal consequence of poorly aerated and atelectatic lung tissue is impaired gas exchange with intrapulmonary shunt formation and a low \( V_{Q}/V_{T} \). In the present study, the high \( \text{PaO}_2 - \text{PaCO}_2 \) gradient (Table 2) detected during the first 60 minutes of anesthesia with mechanical ventilation was compatible with impaired lung aeration; this possibility was considered even more likely because the MAP and heart rate were within respective reference ranges\(^{11}\) reported for sheep (Table 1). The fact that \( \text{PaCO}_2 \) and \( V_{DSS}/V_{T} \) remained within the physiologic range possibly indicates that minute ventilation was adequate and alveolar dead space remained constant throughout the experiments.

Prevention of alveolar collapse and recruitment of alveoli in atelectatic and poorly aerated tissue are important objectives that may prevent pulmonary complications during and after general anesthesia.\(^{30-32}\) Administration of a low \( \text{FiO}_2 \) (ie, 0.3 to 0.6; 30% to 60% oxygen) significantly reduces atelectasis formation in humans and nonhuman animals.\(^{1-4}\) However, ventilation with a low \( \text{FiO}_2 \) is not always applicable in a clinical setting because of technical (eg, lack of a second gas source, lack of control over the oxygen mixture, or inability to monitor \( \text{FiO}_2 \)) or clinical reasons (eg, compromise of lung function prior to surgery). In those circumstances, PEEP and recruitment maneuvers are the only ventilatory techniques available for treatment of anesthesia-related airway closure and atelectasis during surgery.\(^{33-36}\) The term PEEP describes an increased pressure in the airways relative to ambient pressure at the end of expiration. The desired effect of PEEP on the pulmonary parenchyma is to increase FRC as a result of the opening of closed bronchioli and collapsed alveolar units.\(^{30,36,37}\)

In the study reported here, the application of 10 cm H\(_2\)O of PEEP for 20 minutes significantly reduced anesthesia-induced atelectasis (Figures 2 to 4). As expected, alveolar recruitment was primarily in the more caudal lung fields that were most affected by airway closure and atelectasis (Figure 3). Given the lack of any significant time-dependent change in lung aeration, \( \text{PaO}_2 \) remained constant at 1, the effects of PEEP on the \( \text{PaO}_2 - \text{FiO}_2 \) ratio were identical to those on \( \text{PaO}_2 \) (Table 2). In the present study, the high \( \text{PaO}_2 - \text{PaCO}_2 \) gradient (Table 2) detected during the first 60 minutes of anesthesia with mechanical ventilation was compatible with impaired lung aeration; this possibility was considered even more likely because the MAP and heart rate were within respective reference ranges\(^{11}\) reported for sheep (Table 1). The fact that \( \text{PaCO}_2 \) and \( V_{DSS}/V_{T} \) remained within the physiologic range possibly indicates that minute ventilation was adequate and alveolar dead space remained constant throughout the experiments.

It is important to distinguish between PEEP-induced recruitment and \( V_{T} \)-induced alveolar recruitment; these are different events that have different impacts on lung function. Positive end-expiratory pressure is an end-expiratory treatment that is persistent throughout the respiratory cycle. This ensures that alveolar units recruited by PEEP participate fully in gas
exchange (provided that the lung parenchyma is physiologically normal). In contrast, \( V_t \) recruitment is a temporary (ie, inspiratory phase only) event. Although \( V_t \) recruitment may contribute to the improvement of gas exchange, the previously opened lung units collapse again (referred to as derecruitment) during the expiratory phase. The application of PEEP can influence \( V_t \) recruitment as a result of the increase in airway pressure; thus, it is likely that, in the sheep in the present study, there was further improvement of lung aeration during inspiration at \( T_{PEEP} \). To accomplish the objective of this study, however, the authors included an evaluation of PEEP-induced alveolar recruitment. For this reason, CT was performed at end expiration.

The improved gas exchange observed at \( T_{PEEP} \) (Table 2) in sheep in the study reported here emphasizes the positive effect PEEP ventilation has on lung function. In studies\(^{10,11} \) in humans, however, it is cautioned that PEEP-induced improvement of lung aeration may not always be associated with better gas exchange because of the potentially negative impact of PEEP on the pulmonary (ie, redistribution of pulmonary blood flow) and systemic (ie, reduction of cardiac output) circulation. Regarding redistribution of the pulmonary blood flow, even if the \( V/Q \) ratio had not been specifically determined in the present study, the significant improvement in oxygenation and in \( CSTAT \), at \( T_{PEEP} \) supported the premise that 10 cm H\(_2\)O of PEEP improved the \( V/Q \). Regarding systemic hemodynamic function, a possible limitation of the study reported here is that no data were obtained to indicate whether cardiac output was impaired in the sheep. Hemodynamic impairment is an important potential limitation for the application of PEEP during mechanical ventilation in anesthetized patients. In particular, the persistent increase in intrathoracic pressure causes a reduction in venous return; thus, blood flow in the pulmonary and systemic circulation could potentially be reduced.\(^{10} \)

However, clinical studies\(^{12,13} \) in humans and nonhuman animals revealed that in healthy subjects, the cardiovascular compromise imposed by relatively low PEEP (\( \leq 10 \) cm H\(_2\)O) can usually be counteracted with administration of adequate fluids, inotropic drugs, or both. Because MAPs and heart rates remained constant in sheep in the study reported here, we speculate that application of a low PEEP had only minor effects on cardiac output, but we recognize that this aspect deserves further investigation. Moreover, we cannot exclude that the reduction of the \( P_{A\text{O}_2} \) detected in the present study may have been partly attributed to a reduction in the shunt fraction as a consequence of a small reduction in cardiac output induced by PEEP.

Collapsed airways and atelectatic alveoli are usually characterized by higher opening pressures than those required for physiologically normal alveoli; to be recruited (ie, reopened), they require a PEEP high enough to increase the inspiratory airway pressure above the required opening pressure and to prevent recollapse of those units at end of expiration.\(^{10} \) If the PEEP applied is insufficient to accomplish this and alveoli in the atelectatic lung regions cannot be opened, PEEP ventilation fails to recruit lung parenchyma and can potentially result in pulmonary hyperinflation, with PEEP and \( V_t \) disproportionally redistributed to normally aerated lung parenchyma, thereby reducing lung compliance further and impairing gas exchange.\(^{14} \)

On the basis of clinical studies\(^ {32-34} \) in human patients, the most rational and successful approach during those circumstances (ie, failure to recruit the atelectatic alveolar units) is to perform a recruitment maneuver via inflation of the lungs with high inspiratory pressures (eg, 30 to 40 cm H\(_2\)O) for a brief period to recruit as many previously collapsed alveolar units as possible, then to apply a PEEP titrated to a value that will keep alveoli and small airways open. In the group of sheep in the present study, it appeared that the use of PEEP did not induce pulmonary hyperinflation (Figure 2). The opening pressures of alveolar units in atelectatic lung parenchyma are heterogeneous; these vary with the factors described as contributing to atelectasis formation as well as with pathological changes in the lung tissue.\(^ {12} \)

It is important to stress the notion that anesthesiainduced atelectasis usually consists of collapsed alveolar units in healthy lung parenchyma that can easily be recruited and returned to physiologic function.\(^ {8,10} \) The situation is different for pathological pulmonary atelectasis (eg, that which results from acute lung injury, acute respiratory distress syndrome, pneumonia, or tumors), in which inflammatory cell infiltrates, degenerative processes, or both decrease compliance and impair alveolar recruitment.\(^ {80} \)

The application of PEEP should be considered a temporary treatment that is limited to the time that a patient is receiving mechanical ventilation, acting primarily during the end-expiratory phase to address temporary changes of the respiratory system (eg, decreased FRC, airway closure, and pulmonary atelectasis) induced by the anesthetic drugs and techniques. The results of the present study indicated that PEEP improved oxygenation during anesthesia induced and maintained with propofol in healthy sheep ventilated with pure oxygen; application of PEEP also increased FRC via recruitment of atelectatic lung regions. The possible clinical impact of these results in veterinary medicine deserves further investigation, but human data clearly suggest that limiting atelectasis formation during anesthesia is an important step in limiting pulmonary complications during and after surgery.\(^ {5} \)

\begin{itemize}
  \item \textit{a.} Lidocaine 2%, Angelini SpA, Ancona, Italy.
  \item \textit{b.} Midazolam PHG, Hospira, Naples, Italy.
  \item \textit{c.} Propofol 1%, Esteve Hospira Inc., North Chicago, Ill.
  \item \textit{d.} Norcuron 10 mg, NV Organon, Oss, Holland.
  \item \textit{e.} Edwards Lifesciences LLC, Irvine, Calif.
  \item \textit{f.} MiniStim, model MS-II, Life-Tech Inc, Houston, Tex.
  \item \textit{g.} Camsoon, Cambridge Laboratories, Newcastle-Upon-Tyne, England.
  \item \textit{h.} Servo 300, Siemens-Elema, Electromedical System Division, Solna, Sweden.
  \item \textit{i.} Fleish No. 2, Fleish, Lausanne, Switzerland.
  \item \textit{j.} Diff-Cap, Special Instruments, Nordlingen, Germany.
  \item \textit{k.} DAQCard-700, National Instruments, Austin, Tex.
  \item \textit{l.} ICU Lab, Kleis TEK Engineering, Bari, Italy.
  \item \textit{m.} GE ProSpeed Sx, General Electric, New York, NY.
  \item \textit{n.} DicomWorks, version 1.3.3, Cité Internationale, Lyon, France.
  \item \textit{o.} VetStat, IDEXX Laboratories Inc, Westbrook, Me.
\end{itemize}
References


