Lung Volume Recruitment in Lambs during High-Frequency Oscillatory Ventilation Using Respiratory Inductive Plethysmography

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ABSTRACT

Monitoring lung volume is important in the treatment of acute hypoxemic respiratory failure. However, there are no tools available for lung volume measurement to guide ventilator management during high-frequency oscillatory ventilation (HFOV) and during dynamic changes in conventional ventilation (CV). We studied the performance of a new respiratory inductive plethysmograph (RIP) with modified software. We measured Δ changes in lung volume above end-expiratory volume (V_{RIP}) during HFOV and studied whether changes in V_{RIP} parallel changes in mean airway pressure. Calibration of the plethysmograph was made by serial injections of a known gas volume in six term (140 d gestation) and eight preterm (125 d gestation) lambs. Linear regression analysis of the relationship between injected gas volume and V_{RIP} showed strong correlation ($r^2 = 0.93$ –1.00 term animals, $r^2 = 0.86$ –1.00 preterm animals). The pressure volume curves from the calibration with the injected gas volumes also correlated well with the pressure volume curves extrapolated from changes in V_{RIP} . Lung hysteresis was clearly demonstrated with RIP after changes in mean airway pressure during HFOV and after changes in positive end-expiratory pressure during CV. We conclude that measurements of lung volume in term and preterm lambs by use of modified RIP correlate well with changes in mean airway pressure during HFOV, with static pressure volume curves and with changes in positive end-expiratory pressure during CV. We speculate that this technique may provide clinically useful information about changes in lung

volume during HFOV and CV. However, evaluation of the precision and chronic stability of RIP measurements over prolonged periods will require further studies. (*Pediatr Res* 49: 38–44, 2001)

Abbreviations

HFOV, high-frequency oscillatory ventilation
CV, conventional ventilation
PRVC, pressure-regulated volume-controlled
PEEP, positive end-expiratory pressure
 P_{aw} , mean airway pressure
EELV, end-expiratory lung volume
PV, pressure volume
RIP, respiratory inductive plethysmography
 V_{cal} , a known gas volume injected or withdrawn
 V_{RIP} , Δ changes in lung volume above end-expiratory volume at disconnection, measured by RIP
DC, direct current
AC, alternating current
QDC, qualitative diagnostic calibration
RDS, respiratory distress syndrome
bpm, breaths per minute
BP, mean arterial blood pressure
Fio₂, fraction of inspired oxygen
Pao₂, partial pressure of arterial oxygen
Paco₂, partial pressure of arterial carbon dioxide

Monitoring lung volume is important in the treatment of hypoxemic respiratory failure, but few noninvasive tools are available to guide ventilator management. Numerous studies

have demonstrated the importance of monitoring lung volume during mechanical ventilation to improve oxygenation (1–17). Minimizing volutrauma and lung injury is equally important (18–24). Targeting lung volume rather than gas exchange alone may improve survival in patients with acute hypoxemic respiratory failure (25, 26). A reliable noninvasive bedside technique to measure changes in lung volume in response to changes in P_{aw} during HFOV would be an important tool for improving lung volume-targeted ventilation. Lung volume evaluation is important during initial alveolar recruitment and

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after disconnection and suctioning. Efforts have been made to measure lung volumes during HFOV. However, the methods used include interruption of HFOV for nitrogen washout on CV (27) or are too time consuming for measuring rapid dynamic changes (28). Monitoring dynamic changes in lung volume during CV could also be used to modify ventilator settings after changes in PEEP and after surfactant instillation.

RIP is a noninvasive technique for measuring changes in lung volume (29, 30). The method employs thoracic and abdominal elastic bands that register changes in inductance proportional to changes in thoracic and abdominal volume. RIP has been used to measure tidal volume (TV) and minute ventilation and correlates well with pneumotachography in infants and children (31–34). However, measurement of changes in lung volume by use of RIP has been limited by baseline drift and nonlinearity of the measurement at extremes of lung inflation (35).

Recently, software modifications that were designed to allow measurements of lung volume when used in DC-coupled mode were incorporated into a RIP system (RespiTrace, SensorMedics Corp., Yorba Linda, CA, U.S.A.). Our aim with the present study was to determine whether RIP could be used during HFOV and whether RIP measurements of lung volume would respond immediately to changes in P_{aw} and oxygenation. We also studied the immediate changes in lung volume as measured by RIP after changes in PEEP during CV. We hypothesized that V_{RIP} would correlate with changes in V_{cal} . We also hypothesized that changes in V_{RIP} would correlate with dynamic changes in lung volume during recruitment and derecruitment maneuvers on HFOV and during CV of term animals.

In addition to studies during mechanical ventilation of term newborn lambs, we also applied the RIP technique to preterm lambs with severe RDS. Mechanical ventilation of preterm lambs delivered at 125 d (0.85% gestation) provides a natural model of severe RDS caused by surfactant deficiency. This model is characterized by progressive hypoxemia and lung injury during the first hour after delivery and mechanical ventilation (36, 37). In this model of severe RDS, our aim was to correlate V_{RIP} to injections of known gas volumes before and after surfactant treatment. We hypothesized that PV curves extrapolated from RIP measurements would correlate with PV curves from the calibration with injected gas volumes and that these curves would demonstrate less hysteresis in preterm than in term animals. We also hypothesized that increased hysteresis after surfactant instillation could be demonstrated with RIP.

METHODS

The present study was reviewed and approved by the Animal Care and Use Committee at the University of Colorado Health Sciences Center. The handling of the animals was in accord with the guidelines of the National Institutes of Health.

RIP: Technology

RIP is a respiratory transducer that measures the cross-sectional areas of the rib cage and abdomen from changes in electrical inductance. It is composed of two transducers of

Teflon-coated highly flexible and multistranded wires fastened in zigzag form to an elastic band. The zigzag nature of the wire forms the inductance coil for the oscillator electronics. Expansion and contraction of these coils alter the inductance that is converted into proportional voltages by use of a variable frequency oscillator connected to each coil. The signal is isolated with an optocoupler that provides isolation between the oscillator and the subject. The outputs from the optocouplers are sent to phase-locked loops that demodulate the signals and provide DC output signals. These signals are then fed through band-pass filters for the AC-coupled mode and low-pass filters for the DC-coupled mode. The AC-coupled mode has the ability to restore its output to a fixed baseline and allows gains, giving it the maximal dynamic range for TV breathing. The DC-coupled mode is used to reflect changes in resting lung volume (29, 30, 38, 39).

After placement of the RIP bands around the thorax and abdomen, the device is internally calibrated using a QDC procedure. QDC uses a statistical selection of breaths from a calibration period of 5 min. Recent modifications in the software of this device allow assignment of a numerical value for mean lung volume when used in the DC-coupled mode. The RIP was used in DC-coupled mode and was connected to a computer with a serial cable. The measured changes in the electrical inductance were recorded from the computer screen during the study.

Surgical Preparation

Mixed-breed (Columbia-Rambouillet, Nebekar Ranch, Lancaster, CA, U.S.A.) pregnant ewes at either term, 138–147 d gestation (term 147 d), or preterm at 125–126 d gestation (85% of term gestation) were used in this study.

Ewes were sedated with i.v. pentobarbital sodium (2–4 g total dose) and anesthetized with intrathecal tetracaine hydrochloride (1% solution, 3 mg). Ewes were kept sedated with pentobarbital sodium but breathed spontaneously throughout the surgery. Under sterile conditions, a uterine incision was made and the fetal head was exteriorized. After local infiltration with lidocaine, a skin incision was made to expose the trachea, internal jugular vein, and carotid artery. Polyvinyl catheters (20G; Martech Medical Products, Lansdale, PA, U.S.A.) were advanced into the ascending aorta through the carotid artery and into the superior vena cava through the jugular vein. The aortic and jugular catheters were connected to Gould-Statham P23 ID pressure transducers (Gould, Inc., Oxnard, CA, U.S.A.) for pressure measurements. Calibrations of pressure were performed with a mercury column manometer. Pancuronium (0.1 mg/kg) was infused into the fetus, and a tracheotomy was performed with placement of a 3.5-mm internal diameter (ID) (preterm) or 4.0-mm ID (term) endotracheal tube (HiLo Jet Tube, Mallinckrodt Inc., Glenn Falls, NY, U.S.A.). Each animal received an initial infusion of fluid (NaCl 0.9%; 10 mL/kg) followed by a continuous infusion of 5% dextrose in normal saline and pentobarbital ($0.5 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) at 10 mL/h.

Mechanical ventilation was initiated in PRVC mode on a Servo 300 ventilator (Siemens, Solna, Sweden) with Fio_2 1.0

and a set initial TV of 30 mL for term lambs and 25 mL for preterm lambs. The PRVC mode delivers the set TV while minimizing pressure within the limits of ventilatory rate and inspiratory time, detecting compliance changes in the subject. Ventilator rate was set at 30 bpm in term animals and 40 bpm in preterm animals. The inspiratory period was 0.75 s, and the PEEP was set to 6 cm H₂O. Peak inspiratory pressure and P_{aw} were recorded from the ventilator. Ventilator rate, inspiratory time, and F_{iO_2} were kept constant during the entire study. After instrumentation, animals were maintained on a radiant warmer. The RIP bands were placed around the chest and abdomen and secured. The bands were calibrated during CV for all protocols. Animals were killed after the study with high-dose pentobarbital.

Study Design

The study was divided into the four protocols described below.

Protocol 1: Calibration of the RespiTrace with injected gas volumes. The PV curves were performed as follows: after QDC calibration was completed, the tracheotomy tube was disconnected from the ventilator to EELV with 0 PEEP. P_{aw} was monitored using the pressure port of the HiLo jet tube attached to a Bird airway pressure monitor (Bird Products Corp., Palm Springs, CA, U.S.A.). Increments of 20-mL aliquots of air (final volume, 120 mL) were instilled using a syringe in term animals. After each aliquot was instilled, the V_{RIP} value was recorded as well as the airway pressure at the given volume. The deflation limb was characterized in a similar fashion as 20-mL aliquots of air were withdrawn into the syringe. The correlation between V_{cal} and V_{RIP} was studied and presented as V/V curves. This correlation was also shown with PV curves from V_{cal} and the V_{RIP} at the corresponding airway pressure. All volume measurements were presented as volume changes above EELV, which was set to 0. A similar protocol was performed in preterm animals except that 15-mL aliquots were used to a maximal volume of 60 mL.

Protocol 2: Changes in lung volume and oxygenation owing to changes in P_{aw} during HFOV in term animals. The relation between changes in P_{aw} and V_{RIP} was determined during HFOV. Baseline measurements of V_{RIP} were determined after disconnection from the Siemens ventilator before starting HFOV. HFOV (SensorMedics 3100, SensorMedics Inc., Yorba Linda, CA, U.S.A.) was initiated with a P_{aw} of 5 cm H₂O, which was then increased by 5 cm of H₂O at 5-min intervals to a maximum of 35 cm H₂O. P_{aw} was the only ventilator parameter changed in this study. V_{RIP} , airway pressures, arterial blood gas values, and BP were recorded at each P_{aw} level.

Protocol 3: Changes in lung volume and oxygenation owing to changes in PEEP during CV in term animals. We performed PEEP studies during PRVC mechanical ventilation to compare RIP volume changes with changes in oxygenation. PEEP was the only variable changed on the ventilator during this protocol. PEEP was changed at 5-min intervals in increments of 5 cm H₂O to a maximum of 20 cm H₂O. V_{RIP} , airway

pressures, arterial blood gas values, and BP were recorded at each PEEP level.

Protocol 4: Changes in lung volume owing to changes in elastic properties of the lung during CV in preterm animals before and after surfactant instillation. After QDC calibration, the preterm lambs (125 d) were kept on baseline settings of mechanical ventilation as described above (PRVC mode set with a TV of 25 mL, ventilator rate at 40 bpm, inspiratory period of 0.75 s, and a PEEP of 6 cm H₂O; resulting peak inspiratory pressure and P_{aw} were recorded from the ventilator). In three animals, we compared PV curves before and after surfactant instillation to assess whether RIP could detect an acute change in compliance and lung volume. A baseline PV curve before surfactant was performed after the manifestations of RDS became severe [$P_{aO_2} < 13.3$ kPa (100 mm Hg) despite ventilation with F_{iO_2} 1.0]. Surfactant (Infasurf, provided by E.A. Egan, M.D., State University of New York at Buffalo) was then infused over 2–5 min through a side port of the tracheotomy tube during baseline ventilation. A new PV curve was done 30 min after surfactant instillation.

Study Measurements

The value of the electrical inductance obtained from the computer connected to the RIP monitor in this study was called V_{RIP} . V_{RIP} was expressed as the Δ change in the figures to allow grouping of the animals. Ventilator settings and pressures were registered from the ventilators (Servo 300 and SensorMedics 3100). An arterial blood sample was obtained after each change in ventilator settings for measurements of pH, P_{aO_2} , and P_{aCO_2} (Radiometer OSM 3; Copenhagen, Denmark). BP and heart rate were measured throughout the study.

Data Analysis

The injected gas volume per kilogram body weight was plotted against V_{RIP} for term and preterm animals. The relationship between these values during lung inflation and deflation was assessed by linear regression analysis, providing r^2 values. The raw data were presented as V/V curves. PV curves were plotted from V_{cal} and V_{RIP} against the P_{aw} . The EELV when the animals were disconnected from the ventilator was set as the zero point. Data were also plotted as PV curves from term and preterm animals as well as data on preterm animals before and after surfactant instillation. Dynamic changes in V_{RIP} in response to changes in P_{aw} on HFOV were plotted over time along with concomitant changes in P_{aO_2} . A similar plot was made with V_{RIP} and changes in PEEP and P_{aO_2} on PRVC. Linear regression analysis was performed using the computer program StatMost 3.5 (Dataxiom Software Inc., Los Angeles, CA, U.S.A.). Descriptive statistics and graphs were performed with Axum 5.0 (MathSoft International, Bogshot, Surrey, UK).

RESULTS

Fourteen lambs were studied in two groups, six near-term animals (mean gestational age, 140 ± 3 d; term = 147 d; mean birth weight, 3370 ± 290 g) and eight preterm lambs (at 125 d gestation; mean birth weight, 2410 ± 250 g).

Figure 1 shows a trend tracing computed from the RIP signal during a pilot recruitment/derecruitment procedure during HFOV in one animal. It shows the hysteresis of the lungs with an increased lung volume at similar P_{aw} after recruitment.

Protocol 1: Calibration of the RespiTrace with injected gas volumes. Linear regression analysis of the inflation limbs between injected gas volume and the lung volume in the term lambs yielded r^2 values between 0.98–0.99 (Fig. 2a). The r^2 values for the deflation limbs were 0.93–1.00 (Fig. 2b). The r^2 values of the linear regression in the preterm lambs for the inflation limbs were 0.98–1.00 (Fig. 2c) and for the deflation limbs, 0.86–1.00 (Fig. 2d).

The PV curves for both term and preterm lambs with mean values of the P_{aw}/V_{cal} and P_{aw}/V_{RIP} for a given vol/kg demonstrate marked differences in hysteresis between the term (Fig. 3a) and preterm lambs (Fig. 3b).

Protocol 2: Changes in lung volume and oxygenation owing to changes in P_{aw} during HFOV in term animals. Mean changes in oxygenation and V_{RIP} during recruitment and derecruitment maneuvers during changes in P_{aw} in term lambs on HFOV are plotted in Figure 4, a and b. P_{aO_2} increased with each change in P_{aw} up to 25 cm H₂O (Fig. 4a). As P_{aw} was further increased to 35 cm H₂O, V_{RIP} did not increase further, indicating that the lung had been inflated onto the asymptote of the PV curve, and P_{aO_2} fell concomitantly. As P_{aw} was reduced from 35 to 10 cm H₂O, P_{aO_2} increased (Fig. 4b). Marked reduction in thoracic gas volume occurred at a P_{aw} of 5 cm H₂O, reflected as a fall in V_{RIP} and P_{aO_2} . The loss of lung volume was detected by RIP before the deterioration in oxygenation started.

Protocol 3: Changes in lung volume and oxygenation owing to changes in PEEP during CV in term animals. Changes in oxygenation and V_{RIP} during recruitment and derecruitment maneuvers with alterations in PEEP in term lambs during PRVC are shown in Figure 5, a and b. P_{aO_2} increased with each change in PEEP up to 10 cm H₂O (Fig. 5a). As PEEP was increased from 10 to 20 cm H₂O, P_{aO_2} progressively fell, possibly reflecting hyperinflation. P_{aO_2} increased as PEEP was reduced from 20 to 5 cm H₂O (Fig. 5b). Marked reduction in lung volume occurred at a PEEP of 0, reflected as a fall in V_{RIP} and P_{aO_2} . The loss of lung volume was detected by RIP before the deterioration in oxygenation started.

Figure 1. Sample tracing from RIP showing the change in mean thoracic gas volume (V_{RIP}) for changes in P_{aw} in one animal on HFOV.

Figure 2. Regression curves comparing the change in the thoracic gas volume (V_{RIP}) as registered by RIP with V_{cal} during (a) inflation limb/term, (b) deflation limb/term, (c) inflation limb/preterm, and (d) deflation limb/preterm.

Figure 3. PV curves from term animals ($n = 6$) (a) and preterm animals ($n = 8$) (b) with the injected gas volume (mL/kg) $\pm$ SEM on the left y axis ($\bullet$, V_{cal}) and the mean V_{RIP} $\pm$ SEM from the RespiTrace on the right y axis ($\blacksquare$, $-V_{RIP}$). x axis expresses the P_{aw} (cm H₂O) as read from the pressure monitor.

Protocol 4: Changes in lung volume owing to changes in elastic properties of the lung during CV in preterm animals before and after surfactant instillation. The mean values of V_{RIP} and P_{aw} in preterm lambs before and after surfactant treatment are plotted as PV curves (Fig. 6). Surfactant-treated lungs had larger volumes for the same airway pressures during inflation and deflation.

DISCUSSION

In this study, we used RIP to measure relative lung volume (V_{RIP}) changes during HFOV, during CV, and after surfactant replacement in premature animals. Linear regression analysis comparing V_{RIP} with injections of V_{cal} showed good correlation. V_{RIP} also correlated well to changes in P_{aw} on HFOV. As

Figure 4. Parallel changes in mean $P_{aO_2} \pm SEM$ (●) and mean $V_{RIP} \pm SEM$ (▲) in term animals on HFOV during (a) recruitment and (b) derecruitment.

Figure 5. Parallel changes in mean $P_{aO_2} \pm SEM$ (●) and mean $V_{RIP} \pm SEM$ (▲) in term animals on PRVC mechanical ventilation during (a) recruitment and (b) derecruitment.

P_{aw} was decreased, a decrease in lung volume was detected by RIP before severe deterioration in oxygenation occurred.

These findings are important, as HFOV is increasingly used in the management of neonatal and pediatric respiratory failure because of its efficacy in lung volume recruitment without tidal ventilation and without TV-induced lung injury. The use of HFOV with a strategy designed to recruit and sustain adequate lung volume has improved oxygenation in newborns with hypoxemic respiratory failure (40, 41). Lack of success when instituting HFOV is often related to failure in reaching an adequate P_{aw} to cause lung recruitment. However, adverse effects from lung hyperinflation may occur if P_{aw} is not appropriately reduced after lung volume and compliance have improved (19). One previously published study used the combination of an early RIP device and HFOV to detect air trapping during combined HFOV and intermittent mandatory ventilation treatment (42). Monitoring lung volume during HFOV is clinically difficult but remains critical for the successful application of this therapy (12). Of equal importance, measurements of lung volume during HFOV and CV after lung recruitment maneuvers will allow for reduction of P_{aw} without loss of lung

Figure 6. PV curves from preterm animals before (○) and after (■) surfactant instillation ($n = 3$). The y axis represents the mean $V_{RIP} \pm SEM$, and the x axis represents the P_{aw} (cm H₂O) $\pm SEM$ as read from the pressure monitor. Note the left and upward shifting in PV curve and the increased hysteresis after surfactant.

volume by derecruitment (13). Standard methods for static volume measurements, pneumotachography, and indicator gas washout techniques are not applicable to HFOV. This study demonstrates that the application of RIP technology can enhance assessments of lung volume during HFOV.

We also found that dynamic changes in V_{RIP} paralleled changes in PEEP during PRVC ventilation. Although there are several ways to measure static lung volumes on CV, there are some limitations when measuring rapid dynamic responses, and bedside use is cumbersome. The reduction of P_{aw} needed to sustain the same lung volume after surfactant treatment was clearly demonstrated using this technique. In contrast with a previous study (27), we found that there was rapid stabilization of the V_{RIP} signal (within three to five breaths).

Considering the vital role of optimizing lung volume in the management of hypoxemic respiratory failure, the RIP technique has the potential for directly targeting lung volumes and ventilating on the deflation limb of the PV curve during mechanical ventilation. Potential applications of this technique during HFOV include verifying that an effective volume recruitment pressure (P_{aw}) is applied after converting from CV to HFOV. Other potential areas of use are restoring reduced lung volume after disconnection of the ventilatory circuit and providing lung volume measurements when weaning from ventilator support. There are also important implications of RIP measurements when adjusting ventilator settings during CV. Ventilation-induced lung injury is a significant complication of TV ventilation, associated with cyclic stretch stress that precipitates alveolar leak and inflammatory lung injury (26). The technique described in this article may provide critical information about incipient lung overinflation. However, of equal importance is the potential to reduce lung injury caused by insufficient lung recruitment and low functional residual capacity (20). Thus, a lung volume-targeted strategy may offer advantages over the traditional focus on gas exchange alone,

and the technique described here may provide such information in a noninvasive fashion.

Early studies in which older variations of RIP were used have dealt with static lung volume measurements, and they have found good correlation for TV measurements when compared with pneumotachography (31–33, 43–45). However, recent studies in adults have yielded somewhat conflicting results (46, 47). We found good correlation between V_{RIP} and injected gas volumes, perhaps due to the highly compliant chest wall of the newborn. It is possible that lung volume changes are more easily detected by the thoracic bands of the RIP system in the newborn compared with the adult. Edberg *et al.* (8) have shown an increased resting volume after surfactant instillation in preterm babies that could not be seen in our study. This difference is probably due to differences in the technique of establishing the resting volume. In the study by Edberg *et al.* (8), this volume was measured by means of a nitrogen washout technique in a face-out whole body plethysmograph without disconnection of the tracheal tube from the ventilator, whereas, in our study, the EELV was established through disconnection of the tube from the ventilator. This may explain why we did not see an increase in EELV after surfactant, as we may have lost the gained resting volume whereas they did not. The increase in lung compliance is nevertheless clearly shown with the RespiTrace, and a much lower P_{aw} was needed to recruit the lungs after surfactant.

There are several limitations of this technique. Changes in thoracic and/or abdominal band position may change the baseline V_{RIP} recording. Also, the RIP system works with a Wheatstone bridge and bands, which are sensitive to changes in ambient temperature. Environmental temperature fluctuations may affect the resistance of the bridge, which could influence recorded changes in lung volume even in the DC-coupled mode. In the system we tested, the oscillatory module has been moved into the electronic enclosure to protect it from the changes in environmental temperature. However, the effect of ambient temperature on the thoracic and abdominal bands must be considered when monitoring infants nursed under radiant warmers. It is also important to stress that the changes in lung volume inferred from the changes in electrical inductance with RIP are relative and not absolute.

We conclude that acute measurements of lung volume by use of modified RIP technology parallel well changes in P_{aw} during HFOV and also with rapid dynamic changes during CV. We speculate that this technique may provide clinically useful information about acute changes in lung volume, especially during nonconventional non-TV mechanical ventilation. However, determinations of precision and chronic stability of the technique over longer duration require further studies.

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