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Pulmonary Artery Pressure: An Intraoperative Guide to Limiting Resection Volume[1]

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Lung volume reduction surgery (LVRS) has shown promising results in severe emphysema. However, intraoperative indicators are needed to define optimal resection volumes. Diffusing capacity (D_LCO) worsens with larger LVRS and may correlate with pulmonary artery (PA) pressure. We hypothesized that there would be a greater increase in PA pressures with larger volume LVRS in an inhaled elastase animal emphysema model. Twenty-one rabbits were induced with 15,000 units of elastase via an endotracheal tube. Four weeks later, bilateral LVRS was performed through a median sternotomy using an endoscopic stapler. PA pressures were measured prior to LVRS, immediately after LVRS, and at sacrifice. Single-breath D_LCO, static pressure–volume relationships, and forced expiratory flows were measured prior to induction and at corresponding times to PA pressures. Systolic PA pressures increased in both groups immediately after LVRS (small: 2.67 ± 9.2 mm Hg, ANOVA, $P = 0.023$; large: 3.8 ± 8.5 mm Hg, $P = 0.002$), and then decreased at time of sacrifice 1 week later (small: 9.43 ± 4.8 mm Hg, ANOVA, $P = 0.053$; large: 5.2 ± 7.3 mm Hg, $P = 0.552$). The decrease, at sacrifice, in PA pressures was greater for small LVRS animals than large LVRS animals. The mortality rate (MR) for the small resection group was 0%, whereas that for the large resection group was 24%. The MR associated with larger LVRS was appreciably greater than that associated with small LVRS. These studies suggest that PA pressures may prove to be a useful intraoperative indicator for limits of resection.

Key Words: **lung volume reduction surgery; pulmonary artery pressure; pulmonary hypertension.**

INTRODUCTION

Emphysema is a chronic progressive disease of the lungs involving destruction of terminal alveoli and associated airway obstruction. Lung volume reduction surgery (LVRS) has shown promising results in severely symptomatic emphysema patients, but considerable investigation is required to optimize patient selection and operative procedures. Pulmonary mechanics may improve by removal of poorly functioning or dysfunctional lung tissue with LVRS. However, it is unclear how much tissue should be removed, and what parameters can be used to judge optimal resection volumes.

Previous research investigating the effects of resection volume on diffusion capacity and pulmonary compliance suggests that there are limits to how much tissue can be removed for optimal response. While some physiological variables improve with larger volume tissue resections, other variables were shown to begin to deteriorate as excessive lung tissue was excised. Therefore, intraoperative parameters must be identified to help guide resection volumes for LVRS. In a New Zealand White rabbit model with elastase-induced emphysema, animals undergoing progressively larger lung volume resection LVRS (greater than 3 g) were shown to have a worsening of their diffusion capacity (D_LCO), while static compliance continued to improve [1]. Thus, reduction in diffusing tissue, or other physiological variables, may limit the extent of surgical resection that can be tolerated. Unfortunately accurate diffusion capacity may not be obtainable until after recovery from the operation, and there are currently no other intraoperative indicators to define the limits of LVRS resection.

Diffusing capacity in severe emphysema is influ-

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enced by the available gas-exchanging alveolar surface area, ventilation–perfusion matching, and pulmonary capillary blood volume. Decreased pulmonary capillary volume and chronic hypoxemia may be manifested by varying degrees of pulmonary hypertension in patients with advanced emphysema. For these reasons, we hypothesize that pulmonary artery pressures will rise with more extensive pulmonary resections in this animal emphysema model. Such rises in pressure could potentially be used as intraoperative guides to individually assess optimal lung resection volume.

No studies have been reported analyzing PA pressures intraoperatively and following recovery for correlation with physiological outcomes after LVRS. In this study, we investigated the effects of large- and small-volume bilateral staple resection LVRS on intraoperative and postoperative PA pressures in a rabbit model of elastase-induced emphysema. We analyze changes in PA pressure with those of D_LCO, compliance, and expiratory flows in attempt to identify potential intraoperative indicators for limits of resection in LVRS.

METHODS

This protocol was approved by the Institutional Animal Care and Use Committee at the University of California, Irvine. All rabbits were cared for in accordance with the NIH Guidelines for the Care and Use of the Laboratory Animal.

Animal preparation. Twenty-three rabbits (3.0–4.5 kg) were anesthetized with a 2:1 mixture of ketamine HCl (100 mg/ml) and xylazine (20 mg/ml) at a dose of 0.75 ml/kg IM. The rabbits were intubated with a 3-mm endotracheal tube and mechanically ventilated (Harvard Apparatus Dual Phase Control Respiratory Pump—Canine, Harvard Co., South Natic, MA) with tidal volume of 50 ml and frequency of 30–40/min. A 20-gauge intravenous catheter was placed in a marginal ear vein for intravenous access. Anesthesia was maintained with 0.3 ml of a 1:1 mixture of ketamine HCl (100 mg/ml) and xylazine (20 mg/ml) given as an intravenous bolus as needed to maintain apnea throughout all procedures.

Induction of emphysema. Emphysema was induced in 23 rabbits under general anesthesia by aerosolizing 15,000 units (7.89 ml) of porcine elastase (Product E1250, Sigma Chemical Co., St. Louis, MO) through the endotracheal tube over approximately 1 h. The nebulizer (Respirgard, Marquest Medical Products, Inc., Englewood, CO) was placed in the inspiratory arm of the ventilator circuit with the tidal volume provided by the ventilator set at zero with the rate of 30 breaths/min. The O_2 flow through the nebulizer was adjusted to maintain the peak airway pressure at 20 cm H_2O, monitored by a pressure gauge placed at the side port of the endotracheal tube, which provided the tidal volume during induction.

Pulmonary function testing. Lung function measurements (lung volumes, expiratory flows, D_LCO, compliance) were obtained at baseline prior to induction of emphysema, immediately preoperatively at 4 weeks following induction of emphysema, and 1 week postoperatively.

Gas dilution lung volumes. The inhalation gases consisted of 93% helium, 26% oxygen, balanced with nitrogen, 0.87% C_2H_2, and 0.28% $C_{18}O$ (Liquid Carbonics Corp., Los Angeles, CA). All gas concentrations were measured continuously with an on-line mass spectrometer (MGA 1100, Perkins-Elmer Corp., Pomona, CA). Analog data were converted to digital information with an AD converter (Keithley System 570, Cleveland, OH) sampling at 20 Hz and stored on an IBM personal computer.

The anesthetized and intubated rabbits were taken off the ventilator and placed in the left decubitus position. The sampling tube of the mass spectrometer was connected to the side port of the end orotracheal tube through which the inspired and expired gas concentrations were continuously measured. A syringe was filled to 60 cc with inhalation gases and connected to the endotracheal tube. A multibreath helium dilution maneuver was performed by manually insufflating and removing 50 cc tidal volume with the syringe for 10 breaths at an approximate rate of 20–30 breaths/min. The initial and final helium concentrations were used to calculate the functional residual capacity (FRC). Two measurements of FRC were obtained at each trial and averaged. The rabbits were returned to mechanical ventilation following each procedure.

Single-breath carbon monoxide diffusion capacity (D_LCO_{SB}). Five-second breath-hold D_LCO maneuvers were performed following the above FRC measurement on each rabbit. All gas concentrations were measured continuously through the mass spectrometer. Sixty cubic centimeters of the inhalation gas was insufflated into the lung through the endotracheal tube and held for 5 s. Thirty cubic centimeters of the inspired volume was then withdrawn and held to measure the gas concentrations at 33% expired volume. All data were sampled and digitized at 20 Hz.

For analysis, the breath-hold time was measured from 0.5 s from the start of inspiration to 30 cc of exhalation. The duration of inhalation was rapid and peak concentrations were achieved within 1 s. The initial helium and $C^{18}O$ concentrations were measured at their respective concentration plateaus following gas insufflation. The final gas concentrations were measured at 30 cc exhalation. D_LCO was calculated from the standard formula and corrected to STPD. Adjustments were made for the rabbit body temperature and water vapor pressure.

Lung volume reduction surgery. LVRS was performed 4 weeks following elastase induction of emphysema. The anesthetized and intubated rabbits were shaved and placed in the supine position. Twenty-three rabbits underwent resection of varying quantities of lung tissue.

Hypothermia was prevented with a surgical warming pad, and lactated Ringers solution was infused through an intravenous catheter in a marginal ear vein at 5–15 cc/h. The rabbits were mechanically ventilated. Oxygen saturation (Ohmeda Biox 3700 Pulse Oximeter, BOC Health Care), tidal CO_2 (Olimeda 5200 CO_2 Monitor, BOC Health Care), and EKG (Hewlett–Packard 78353B Continuous EKG Monitor, BioMedical Services) were monitored continuously.

The chest was shaved, prepped with betadine, and draped sterilely. The thorax was entered through a median sternotomy. Bilateral upper and middle lobes were excised using a linear thoracoscopic stapler (Endopath ELC, Ethicon Endo-Surgery) with 3.5-mm staples. Target quantity of lung tissue removed was 2–6 g. The quantity of excised lung weight was carefully escalated. The excised lung tissue weights were obtained intraoperatively to assess adequate target resection. In the sham operations, no lung tissue was excised. Hemostasis was obtained and a 12-Fr neonatal chest tube was placed under direct visualization into each pleural space. The two chest tubes were connected to 10 cm water suction. The sternum was closed with O silk and the chest wound closed in layers with absorbable monofilament sutures. The rabbits were awakened from anesthesia and extubated. There was usually a small airleak in the chest tubes but all leaks sealed spontaneously within 1 h. All chest tubes were removed within 1 h.

Pulmonary artery pressure measurement. Pulmonary artery pressures were measured in 23 animals by using a cardiac monitor (Hewlett–Packard 78353B Continuous EKG Monitor) connected to a transducer attached to a standard-pressure saline bag. The saline bag pressure was raised to 200 mm Hg and then the transducer was zeroed at the level of the pulmonary artery and calibrated. After the median sternotomy was performed and the catheter zeroed, the

TABLE 1

Pulmonary Artery Pressures

	Group I			Group II		
	Pre-LVRS (n = 10)	Post-LVRS (n = 9)	Sacrifice (n = 9)	Pre-LVRS (n = 10)	Post-LVRS (n = 9)	Sacrifice (n = 9)
Systolic pressure (mm Hg)	16.4 ± 4.3	22.5 ± 4.2	13.25 ± 3.3	17.7 ± 5.5	25.5 ± 7.0	19 ± 2.4
Diastolic pressure (mm Hg)	8.5 ± 3.2	10.25 ± 2.8	5.75 ± 2.4	8.6 ± 3.9	12.6 ± 5.4	9.9 ± 1.6
Mean pressure (mm Hg)	10.82 ± 3.1	14.33 ± 3.1	8.25 ± 2.3	11.67 ± 4.3	11.7 ± 5.8	12.93 ± 1.3

measurement was taken by using a 24-gauge catheter. Pulmonary artery pressures were measured while the thorax was open. The catheter was inserted into the right ventricular outflow tract and advanced into the pulmonary artery. When the characteristic PA waveform was visualized on the monitor the measurements were obtained. Measurements were performed before LVRS and then repeated after LVRS and at sacrifice 1 week later. Measured parameters included systolic and diastolic PA pressures. The mean PA pressure was calculated using the standard formula: MPAP = (2PAD + PAS)/3.

Histologic preparation. The animals were sacrificed 1 week following LVRS. The lungs were removed en bloc and inflated with formalin (20 cm pressure) for histological preparation. The lung sections were prepared at 0.2- to 0.4-cm thickness and embedded in paraffin. Slides were stained with hematoxylin–eosin and studied by light microscopy.

Animal analysis groups. Animals were separated into two groups for analysis. Low resection volume (<3 g) constituted the first group, while the second group was high resection volumes (>3 g).

Statistical analysis. All helium dilution lung volume, compliance, flow, and D_LCO data for each rabbit were tabulated corresponding to baseline, preoperative, and postoperative measurements. Comparisons of baseline to preoperative values and preoperative to postoperative values were made using paired two-sample ANOVAs. Comparisons of response to surgery based on treatment groups were made using unpaired two-sample ANOVAs. A standard statistical software program was used for all statistical analysis (Systat 7.0, SPSS Inc.). The change in D_LCO from preoperative to postoperative data was analyzed and graphed in relation to the excised lung weights.

RESULTS

Emphysema was induced and the rabbits underwent LVRS the fourth week after induction. The mortality rate from elastase induction was 10.8%. The mortality rate after LVRS was 15%. All of the deaths occurred in the large resection group. None of the postoperative deaths occurred in the small resection group. The postoperative mortality in the large resection group alone was 24%. Resected lung volumes ranged from 1.9 to 6.39 g. Animals in the small resection group had a mean resection volume of 2.31 g (±0.298 g). Animals that survived in the large resection group had a mean resection volume of 4.34 g (±0.63 g). The average tissue resection volume in the animals that died was 4.36 g. The rabbits that died postoperatively tended to expire 2 to 3 days after surgery. Autopsy performed after death revealed delayed pneumothoraces in all cases.

Pulmonary Artery Pressure

Systolic PA pressure. Systolic PA pressures were measured in all rabbits before and after LVRS and at sacrifice. The average systolic pressure in the small resection group pre-LVRS was 16.4 mm Hg (±3.4 mm Hg); post-LVRS, 22.5 mm Hg (±4.2 mm Hg); and at sacrifice, 13.25 mm Hg (±3.32 mm Hg). The average change in systolic PA pressure in the small resection group from pre-LVRS to post-LVRS was 2.67 mm Hg (±9.2 mm Hg). The average decline in systolic PA pressure from surgery to sacrifice in the small resection group was 6.2 mm Hg (±4.2 mm Hg). The average systolic PA pressure in the large resection group pre-LVRS was 17.7 mm Hg (±5.5 mm Hg); post-LVRS, 25.5 mm Hg (±6.9 mm Hg); and at sacrifice, 19 mm Hg (±2.4 mm Hg). The changes in pressure in the small resection group were compared with the pressure changes seen in the large resection group, 3.8 and −5.2 mm Hg, and were noted to be not significant. The change in systolic pressure from pre-LVRS to post-LVRS was significant in both groups (ANOVA, P = 0.023, P = 0.002). The change from post-LVRS to sacrifice was also noted to be significant in the small resection group while only approaching significance in the large resection group (ANOVA, P = 0.002, P = 0.065) (see Table 1). The systolic PA pressure was measured in only one of the animals that died because we did not institute PA measurement in this series of animals until later in the study. In this animal the systolic PA pressure increased by 17 mm Hg after LVRS.

Diastolic PA pressure. Diastolic PA pressures were measured in all rabbits before and after LVRS and at sacrifice. The average diastolic pressure in the small resection group pre-LVRS was mm Hg (±3.2 mm Hg); post-LVRS, 10.25 mm Hg (±2.8 mm Hg); and at sacrifice, 5.75 mm Hg (±2.43 mm Hg). The average change in diastolic PA pressure in the small resection group from pre-LVRS to post-LVRS was 1.1 mm Hg (±5.1 mm Hg). The average decline in diastolic PA pressure from surgery to sacrifice in the small resection group was 4.25 mm Hg (±4.1 mm Hg). The average diastolic PA pressure in the large resection group pre-LVRS was 8.64 (±3.9 mm Hg); post-LVRS, 12.6 mm Hg (±5.4 mm

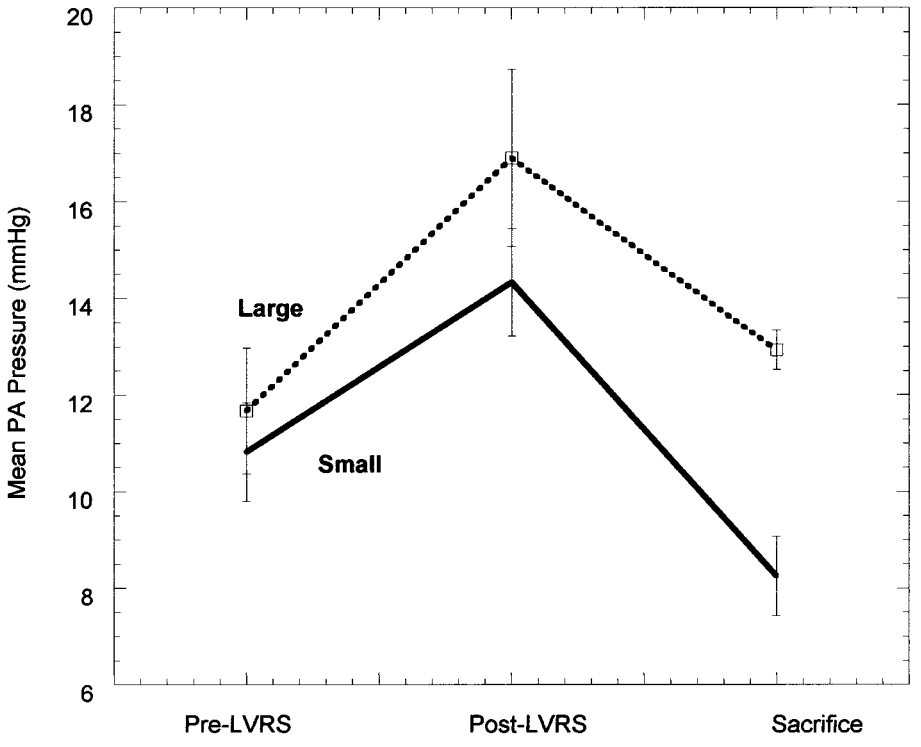

FIG. 1. Mean pulmonary artery pressure with LVRS. Graph of MPAP for small and large resection groups taken at three different times: pre-LVRS, post-LVRS, and sacrifice. PA pressures tend to rise in both groups after LVRS and then fall at time of sacrifice. A greater fall is seen in the small resection group, while pressures remain elevated in the large resection group.

Hg); and at sacrifice, 9.9 mm Hg (±1.6 mm Hg). The changes in pressure in the small resection group were compared with the pressure changes seen in the large resection group, 2.8 and −0.5 mm Hg, and were noted to be not significant. The change in diastolic pressure from pre-LVRS to post-LVRS was not significant in the small resection group but significant in the large resection groups (ANOVA, $P = 0.358$, $P = 0.014$). The change from post-LVRS to sacrifice was noted to be significant in the small resection group while not significant in the large resection group (ANOVA, $P = 0.032$, $P = 0.360$) (see Table 1). The diastolic PA pressure in the animal that died postoperatively increased by 20 mm Hg.

Mean PA pressure. The mean PA pressure increased immediately after LVRS and then decreased from LVRS to surgery (see Fig. 1). The average increase in mean PA pressure in the small resection group was 3.12 mm Hg (±4.6 mm Hg) while in the large resection group the average increase was 5.2 mm Hg (±4.4 mm Hg). The average decline in mean PA pressure in the small resection group was 6.2 mm Hg (±4.2 mm Hg) while that of the large resection group was 2.85 mm Hg (±5.7 mm Hg) (see Table 1). The change in mean PA pressure from pre-LVRS to post-LVRS was greater in the large resection group by a factor of 1.7 (ANOVA, $P = 0.23$) (see Fig. 2). The mean PA pressures from pre-LVRS to sacrifice were significantly different between the two groups (ANOVA, $P = 0.046$) (see Table 2). The mean PA pressure in the animal that died postoperatively increased by 19 mm Hg.

D_LCO

The single-breath D_LCO decreased in both groups after LVRS but the change did not reach statistical significance (ANOVA, $P = 0.14$, $P = 0.27$) (see Fig. 3). There was no difference between the two groups (ANOVA, $P = 0.69$) (see Table 3).

Flow

Early forced expiratory flows were assessed at 33% of expired volume. The flow increased in the large resection group (ANOVA, $P = 0.69$) while it decreased in the small resection group (ANOVA, $P = 0.04$) with LVRS (see Fig. 4). The flows at sacrifice were significantly different between the two groups (unpaired t test, $P = 0.003$) (see Table 3).

Compliance

Static respiratory system pressures at maximum insufflation (60 cc) were noted to decrease with induction of emphysema and then increase with LVRS in both groups (see Fig. 5). A greater increase was seen in the

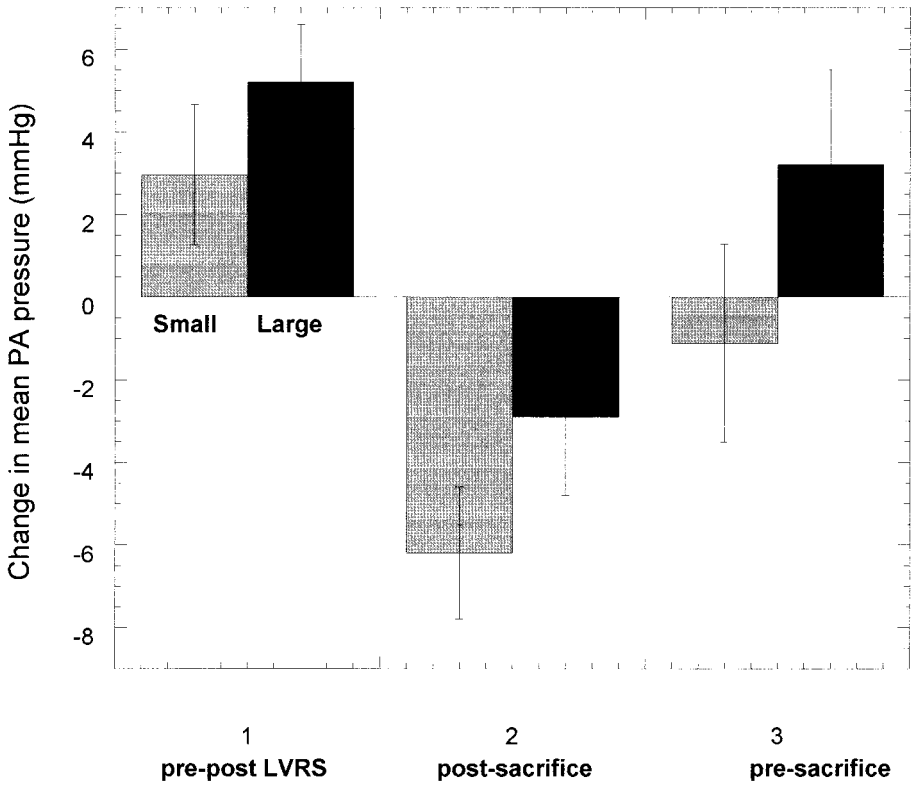

FIG. 2. Change in mean PA pressure with LVRS. The graph shows the average change in MPAP in small and large resection groups from pre-LVRS to post-LVRS, post-LVRS to sacrifice, and pre-LVRS to sacrifice.

large resection group than in the small resection group. The change was considered statistically significant in both groups at the time of sacrifice (ANOVA, $P < 0.05$, $P < 0.05$) (see Table 3).

DISCUSSION

Lung volume reduction surgery is performed for palliation of severe emphysema with little objective intraoperative information to guide optimal volume of lung to be resected. In emphysematous patients undergoing this procedure approximately 30% of the bilateral upper lung fields are removed as assessed by clinical estimation of operating surgeons. Efforts have been made to target particular areas of more advanced disease with preoperative imaging studies in heterogeneously distributed emphysema presentations. The major goal of this research study is to develop methods for determining optimal LVRS resection volumes.

LVRS procedures are generally performed in high-risk patients, with acute mortality rates of 3–5% in most reports and morbidity approaching 10–20% in several studies [2–4]. Objective intraoperative indicators for limits of resection are needed to optimize outcomes following LVRS. Previous animal studies have demonstrated that diffusing capacity worsens with larger resection volumes and could potentially help guide limits of resection volume. However, D_LCO is difficult to accurately measure intraoperatively for technical reasons (high inspired F_IO_2, mechanical ven-

TABLE 2

Change in Pulmonary Artery Pressure with LVRS

	Pre-LVRS to Post-LVRS			Post-LVRS to sacrifice			Pre-LVRS to sacrifice		
	Group 1 ($n = 9$)	Group 2 ($n = 9$)	P value	Group 1 ($n = 9$)	Group 2 ($n = 9$)	P value	Group 1 ($n = 9$)	Group 2 ($n = 9$)	P value
Systolic pressure (mm Hg)	2.67 ± 9.2	3.8 ± 8.5	>0.05	−9.43 ± 4.8	−5.2 ± 7.3	>0.05	−3.71 ± 3.3	1.1 ± 7.5	>0.05
Diastolic pressure (mm Hg)	1.1 ± 5.1	2.8 ± 5.9	>0.05	−4.25 ± 4.1	−0.5 ± 6.1	>0.05	−2.25 ± 4.3	1.6 ± 3.9	0.067
Mean pressure (mm Hg)	3.12 ± 4.6	5.2 ± 4.4	>0.05	−6.2 ± 4.2	−2.85 ± 5.7	>0.05	−1.12 ± 6.7	3.2 ± 7.1	0.046

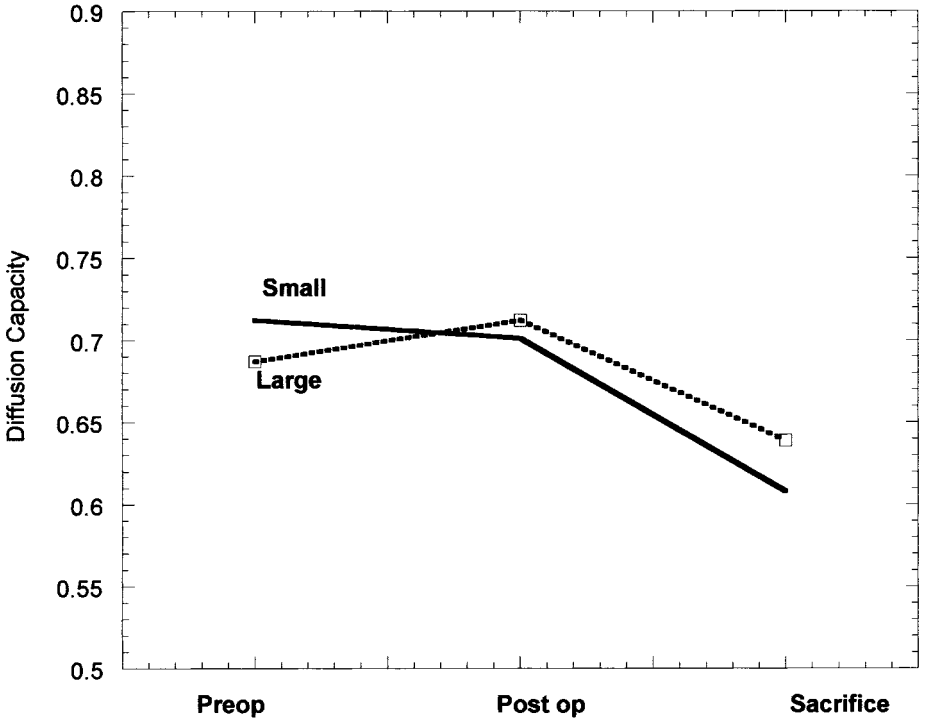

FIG. 3. Diffusion capacity with LVRS. Diffusion capacity for small and large resection groups at baseline, preoperatively, and postoperatively at sacrifice.

tilation) as well as operative conditions that may acutely decrease D_LCO (atelectasis, bronchospasm, secretions, and positive-pressure ventilation). Therefore, we chose to investigate other potential intraoperative physiological measures that may be more applicable to LVRS outcome optimization.

D_LCO is determined by pulmonary capillary circulation, alveolar surface area and thickness, and ventilation–perfusion relationships. Since D_LCO appears to be sensitive to LVRS volumes, we hypothesized that removal of excessive lung tissue would also result in impaired pulmonary circulation, manifested by increased PA resistance and pressures. Pulmonary artery pressures can be measured intraoperatively and can be followed throughout the operative procedure.

Little information is available at this time regarding the effects of LVRS on pulmonary artery pressures. In a case reported in the Japanese literature, one patient was noted to have marked elevation of his pulmonary artery pressure after LVRS [5]. He subsequently had normalization of his PA pressure several months later.

We investigated whether PA pressures correlate with D_LCO changes and physiological outcome variables to assist in determining intraoperative parameters for limits of resection. The data demonstrate that pulmonary artery pressures increased in both high and low resection volume treatment groups immediately after LVRS, and then decrease at the time of sacrifice 1 week later. The decrease in PA pressures from immediately after surgery to sacrifice is significantly larger for animals undergoing small volume resection than following large volume resection.

TABLE 3

Pulmonary Function Tests in Large- and Small-Volume LVRS

	Group I			Group II		
	Baseline	Preoperative	Postoperative	Baseline	Preoperative	Postoperative
D_LCO	0.712 ± 0.21 (n = 9)	0.701 ± 0.17 (n = 9)	0.608 ± 0.13 (n = 8)	0.687 ± 0.19 (n = 11)	0.712 ± 0.18 (n = 11)	0.639 ± 0.13 (n = 9)
FEF33	249.8 ± 61.6 (n = 7)	134.98 ± 31.1 (n = 9)	83.69 ± 31.4 (n = 8)	216.44 ± 74.3 (n = 10)	170.24 ± 47.8 (n = 10)	208.92 ± 90.3 (n = 9)
Static respiratory pressure	18 ± 2.3 (n = 9)	17 ± 1.7 (n = 9)	19.1 ± 2.9 (n = 9)	18.9 ± 1.5 (n = 11)	17.4 ± 1.8 (n = 11)	22.25 ± 2.3 (n = 8)

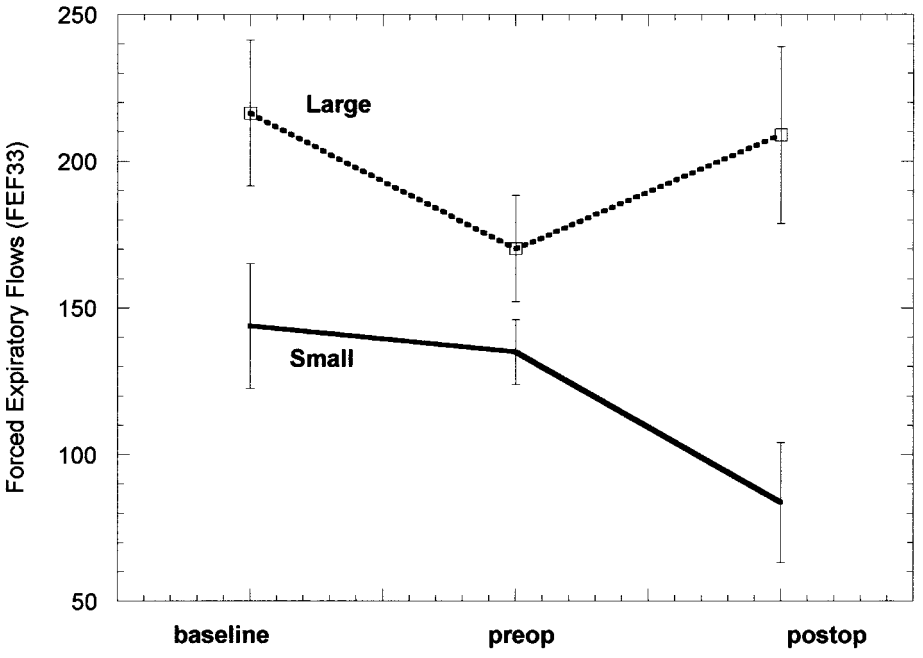

FIG. 4. Forced expiratory flows with LVRS. Graph of forced expiratory flows for small resection group and large resection group measured baseline, preoperatively, and postoperatively at sacrifice.

West [6] described alveolar crowding and collapse of pulmonary capillary beds with increased resistance to flow within the capillary vessels during positive-pressure exhalation. As the lungs expand, the capillary walls are stretched and pulmonary vascular resistance decreases. With lung volume reduction surgery the removal of lung tissue functionally increases recoil pressure, decreasing intrathoracic pressure at equivalent lung volumes. This could account for some of the decrease seen in the PA pressure after the recovery period from LVRS following small volume resections. With larger volume resections the lungs may no longer be able to compensate by increased capacitance of the remaining vessels. This could account for the rise in

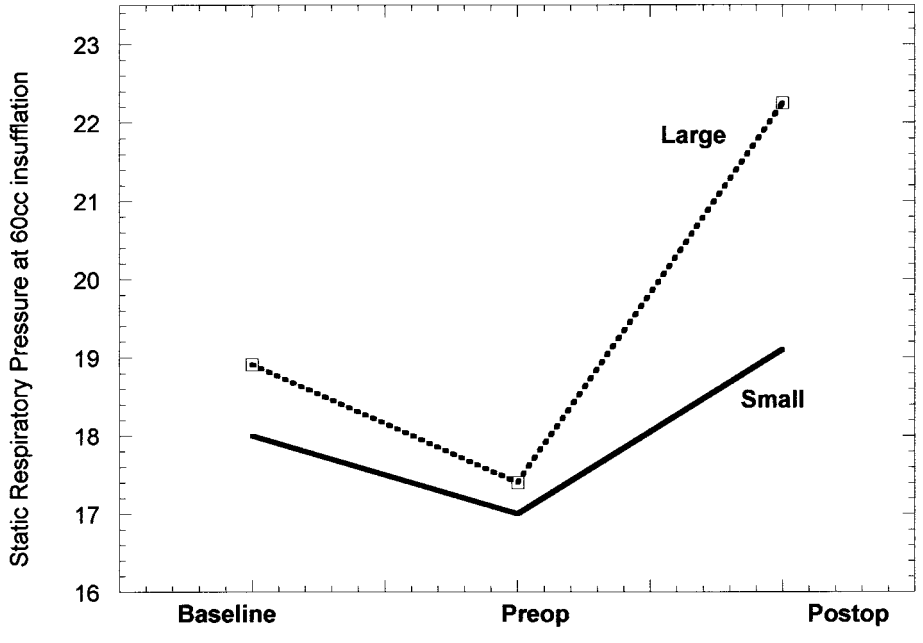

FIG. 5. Static respiratory system pressures with LVRS. Static respiratory system pressures for small and large resection volumes at baseline, preoperatively, and postoperatively at sacrifice.

pulmonary artery pressures after recovery following the larger volume resections. In patients with baseline pulmonary hypertension, this raises concerns about risks of sustained pulmonary hypertension and right-sided heart failure following excessive lung tissue removal.

In this model, pulmonary artery pressure rises that are seen following large volume resections suggest that PA pressures could limit the extent of tolerable surgery, in a manner analogous to falls in D_LCO with larger volume resection. This contrasts with concurrent compliance measurements and expiratory flows, where larger volume resections are associated with normalization of compliance curves and improved flow. Thus, improvements in some physiological markers must be weighed against deterioration in other parameters as resected volumes increase during LVRS.

Interestingly, intraoperative PA pressure immediately following LVRS increased by a similar amount in both small and large volume resections. The increases are likely due to a number of acute operative factors including atelectasis, increased positive airway pressures (since ventilation volumes were maintained constant), and acute airway disease (bronchospasm). Thus, while this information is useful for physiological understanding of the effects of LVRS on cardiopulmonary function, it is only after postoperative recovery that differences in PA pressures are detected between large and small volume resections. Therefore, if PA pressures are to be a useful intraoperative indicator of optimal extent of resection, methods must be developed for differentiating the extent of irreversible PA pressure rise from reversible intraoperative pressure rise. Standardizing inhalation to equivalent pressures (not volume) during PA pressure measurements and use of bronchodilators or inhaled NO during PA pressure evaluations could help distinguish reversible from irreversible intraoperative PA pressure increases.

Rabbits that underwent large volume resection had elevated PA pressure 1 week after LVRS compared with preoperative levels, while the rabbits with small volume resections had decreased PA pressures 1 week after LVRS. Both pulmonary vascular resistance and cardiac output determine PA pressures. It is possible that some of the changes in PA pressure from the immediate postoperative period to 1 week later (presacrifice) could be due to changes in cardiac output. During the LVRS procedure the animals receive lactated Ringers solution at a rate of approximately 10 cc/h. It is possible that animals had lower intravascular volumes and consequently lower cardiac outputs at the time of sacrifice compared with immediately after surgery. While this might explain the fall in pressure below baseline, it would not account for difference in sacrifice PA pressures between the large and small volume resection treatment groups. Additionally, indirect indicators of cardiac output, blood pressure, and heart rate were similar in all cases. Nonetheless, we cannot make definitive statements regarding the role of cardiac output and its effects on PA pressures at this time. Future studies examining cardiac output in this model may help to answer this question.

While PA pressures may eventually be an intraoperative tool to help determine how much tissue to remove, there are a number of other serious limitations to this approach that can be seen from this study. All PA pressure measurements were made in anesthetized rabbits with open chests under positive-pressure ventilation. Such measurements may not accurately reflect the normal physiological properties of the animals when the thorax is closed under negative-pressure inspiratory conditions. The animals had normal pulmonary artery pressures preoperatively despite emphysema. This may be due to the acute nature of the disease process since pulmonary hypertension may take considerable time to develop or a lower severity of emphysema involvement than in many operative patients. Pulmonary artery pressure limitations of resection volumes may be much more marked if baseline PA pressures had been elevated. Additionally, all measurements were made at rest. Since pulmonary artery pressures are extremely dependent on cardiac output when capacitance reserve is exhausted, exercise PA pressures may be much more critical determinants of resection volume limits than resting measurements. Future work is clearly needed to address these important issues.

There are a number of clear differences in presentation and physiology between this model and chronic severe emphysema in humans. However, there are many physiological properties that are similar, and the investigations we focus on are those that are expected to respond analogously. In humans it would be impossible to determine the absolute maximal tolerable resection volumes or which physiological variables limit the extent of resection that subjects are capable of surviving. The difference between the acute disease that we developed and the chronic disease that humans exhibit does not appear to be in lung parenchyma, but more likely in pulmonary vasculature and chest wall physiology. The chronic pulmonary vascular adaptations to reduced capillary cross-sectional area likely take a number of years to develop in patients. Animals induced acutely do not manifest the pulmonary hypertension that may be seen in chronic emphysema patients. We also know that in humans, the chest wall is less compliant. The chest wall of rabbits is more compliant and, therefore, would not be expected to respond analogously to that of human emphysema patients. However, our group and others have shown that the chest wall itself may not contribute significantly to the physiological response to LVRS [7].

Overall, this study has shown that pulmonary pressures rise following large volume LVRS in an animal model, and provides insights into potential limiting factors for the optimal extent of tissue removal during LVRS. This study also shows that the mortality rate associated with larger volume LVRS is appreciably larger than that of small volume resection, 24% versus 0%. This further supports the idea that there is a limit to lung resection volume and this limit can be demonstrated not only by a compromise in the diffusion capacity but also in survival. However, a number of issues must be resolved in future investigations before the role of PA pressures or other objective physiological variables can be used clinically to guide resection extent in patients undergoing LVRS for palliation of severe emphysema.

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