NOTE TO USERS

DISSERTATION

ONE-LUNG VENTILATION IN DOGS. EFFECT OF POSITIVE END-EXPIRATORY PRESSURE ON OXYGEN DELIVERY WITH CLOSED AND OPEN CHEST

Submitted by

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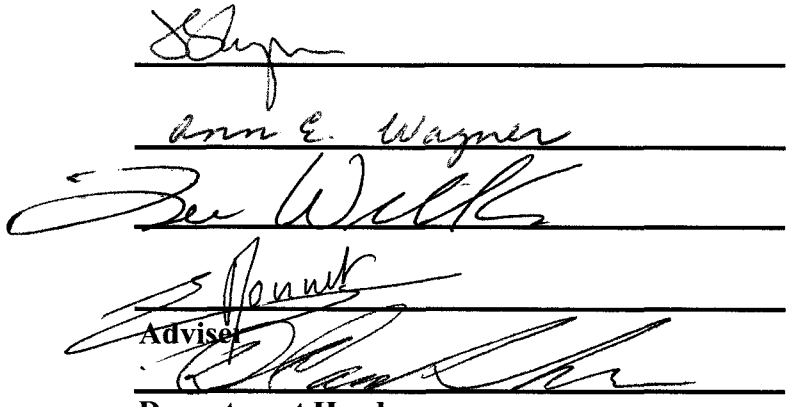
WE HEREBY RECOMMEND THAT THE DISSERTATION PREPARED UNDER OUR SUPERVISION BY MIRIAM RIQUELME ENTITLED ONE-LUNG VENTILATION IN DOGS. EFFECT OF POSITIVE END-EXPIRATORY PRESSURE ON OXYGEN DELIVERY WITH CLOSED AND OPEN CHEST BE ACCEPTED AS FULFILLING IN PART REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY.

Committee on Graduate Work



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ABSTRACT OF DISSERTATION

ONE-LUNG VENTILATION IN DOGS. EFFECT OF POSITIVE END-EXPIRATORY PRESSURE ON OXYGEN DELIVERY WITH CLOSED AND OPEN CHEST

Selective ventilation of one lung (OLV) significantly decreases PaO_2 and SaO_2, and increases Q_S/Q_T. A rapid way to improve oxygenation during OLV is PEEP.

The ultimate variable to evaluate oxygenation of peripheral tissues and vital organs is DO_2. The objective of this research is to evaluate the effects of OLV and PEEP in dogs on DO_2 with closed and open chest.

Seven clinically normal adult dogs were anesthetized and catheters were inserted in the dorsal pedal and pulmonary arteries. Dogs were positioned in right lateral recumbency. After reaching baseline ($PaCO_2$ of 35 to 45 mm Hg), data was collected for closed chest during TLV, and OLV with 0 PEEP, $PEEP_{2.5}$ and $PEEP_5$. Two-lung ventilation with 0 PEEP was resumed, and after a left thoracoscopic approach, the same set of data was retrieved for open chest. An equilibration period of 15 minutes was allowed before collection of data for each point. Statistical analysis was done with an ANOVA for repeated measures.

During closed chest, OLV induced a significantly increased Q_S/Q_T ($P = 0.002$), and reduced PaO_2 ($P < 0.001$), SaO_2 ($P = 0.002$), and CaO_2 ($P < 0.001$). Cardiac

index was not altered, resulting in nonsignificant changes in DO_2.

Positive end-expiratory pressure during closed chest OLV significantly decreased Q_S/Q_T ($P = 0.015$) and increased SaO_2 ($P = 0.022$). However, it failed to significantly affect CaO_2 or CO. Thus, DO_2 was not significantly affected.

Interaction between OLV and closed-open chest was significant for Q_S/Q_T ($P = 0.034$), PaO_2 ($P = 0.006$), CaO_2 ($P = 0.005$), and P_A-aO_2 ($P = 0.008$), but not for SaO_2 ($P = 0.211$). Other cardiopulmonary variables were not affected. As a net result DO_2 was not significantly altered.

Interaction between OLV-$PEEP_{2.5}$-$PEEP_5$ and closed-open chest was significant for PAWP ($P = 0.010$) and MPAP ($P = 0.004$), but it did not affect other variables. As a net result DO_2 was not significantly changed.

It was concluded that OLV and the use of $PEEP_{2.5}$ and $PEEP_5$ during OLV in anesthetized healthy dogs with a closed or open thoracic cavity does not affect DO_2.

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DEDICATION

This dissertation is to Dr. Eric Monnet, for his great spirit and inspirational lessons. To Dr. Rafael Alonso Amelot († 2000), my earliest source of inspiration, teacher and adviser, and to Dr. Alan Tucker († 2004), my teacher and former member of my tutorial committee.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF KEY WORDS

1. One-lung ventilation
2. Positive end-expiratory pressure
3. Oxygen delivery
4. Shunt fraction
5. Cardiopulmonary
6. Thoracoscopy

CHAPTER I

INTRODUCTION

Thoracoscopy is a minimally invasive surgical technique that has been used to explore and perform operative procedures in humans and animals. It is associated with decreased postoperative pain and morbidity.

Minimally invasive surgery is becoming increasingly popular. For thoracic surgery, as thoracoscopic procedures evolved replacing many traditional surgical thoracotomies, it became mandatory to have better visibility and immobility of intrathoracic structures to facilitate precision and surgical access. One-lung ventilation allows immobilization and collapse of the lung on the side of the surgical approach while ventilation is limited only to the nonoperative lung.

Thoracoscopy can also be performed with CO_2 insufflation while keeping both lungs ventilated. Given that CO_2 insufflation collapses the lung through an increase in intrathoracic pressure, it induces a profound cardiovascular compromise with important hemodynamic consequences; OLV is superior in terms of surgical visibility and hemodynamic stability, compared with insufflation with CO_2.

One-lung ventilation was first described in 1936. Originally it was intended to prevent transbronchial spread of disease during lung resections. Currently, in addition to its use in preventing involvement between the affected lung to its counterpart, it is the

standard technique for thoracoscopic procedures.

Conversion from TLV to OLV causes significant decreases in PaO_2 and SaO_2 and a significant increase in Q_S/Q_T mainly as a result of continued blood flow through the nonventilated lung.

The ultimate variable to evaluate oxygenation of peripheral tissues is DO_2. It requires integration of the respiratory, cardiovascular, and microvascular systems, and it is a function of CO and CaO_2. The effect of OLV on DO_2 has been assessed in a limited number of studies. Hemodynamic and pulmonary variables have been studied together but have not been integrated to calculate DO_2.

The net effect of OLV on DO_2 has not been evaluated in situations involving a closed thoracic cavity. Chapter IV describes the respiratory and hemodynamic changes induced by use of OLV in anesthetized dogs with a closed thoracic cavity, and calculates DO_2 as a more accurate assessment of the actual availability of oxygen to tissues.

Maneuvers like the application of continuous positive airway pressure to the nonventilated lung, increase in V_T, and application of PEEP to the ventilated or nonventilated lung have been used to prevent hypoxemia during OLV. Some of these techniques however have disadvantages such as interfering with visibility and interrupting immobility of the thoracic structures over the surgical side.

Positive end-expiratory pressure opposes the tendency for lung atelectasis by keeping airway and alveolar pressures positive at the end of the expiration and increasing FRC. Because during OLV, atelectatic areas in the ventilated lung, as a result of positioning, anesthesia and paralysis, also contribute to the increase in Q_S/Q_T and impairment of oxygenation during OLV, the application of PEEP to the ventilated lung has been used as a rapid way to improve oxygenation during OLV.

The effect of PEEP depends on different factors such as the amount of PEEP that is being applied, the compliance of the lungs, and the oxygenation status of the patient before the application of PEEP. High amounts of PEEP may result in negative hemodynamic effects. Chapter V describes the respiratory and hemodynamic changes and the effect on DO_2 induced by use of low levels of PEEP (2.5 and 5 cm H_2O) in the ventilated lung during OLV in anesthetized dogs with a closed thoracic cavity.

Important elements such as venous return affecting CO, and transpulmonary pressure counteracting the collapse of the lungs, are dependent on intrathoracic pressure. The normal negative intrathoracic pressure within a closed chest is lost when the thorax is open. Opening the thoracic cavity results in further collapsed areas of the lung in addition to those caused by anesthesia, positioning and paralysis. On the other hand, part of the negative hemodynamic effects of PEEP are related to an increase in intrathoracic pressure that is proportional to the amount of PEEP that is being used. This effect therefore may vary depending on the chest being closed or open.

Chapter VI describes the behavior of the cardiorespiratory variables and DO_2 during OLV in the closed-open chest situation through the evaluation of the interaction of these factors.

Chapter VII analyzes the interaction between the use of PEEP during OLV and closed-open chest to describe the variations of the respiratory and hemodynamic variables and DO_2.

CHAPTER II

ONE-LUNG VENTILATION REVIEW

A. INTRODUCTION

One-lung ventilation is the isolation and selective ventilation of one lung.[1] It was first described by Gale and Waters in 1931[2] and then by Magill in 1936. Originally, it was intended to prevent transbronchial spread of disease during lung resections by the use of an endobronchial anesthetic tube with an inflatable rubber cuff.[3,4] Later in 1938 thru 1949, techniques using occlusion of the main bronchus to the diseased lung were described.[5-8] One of the complications with these methods was the inability to deflate the lung in the operative side, making the intervention more difficult.[9]

There are absolute and relative indications for OLV.[1] Absolute indications are situations in which failure to separate the lungs could be life-threatening. These indications include the prevention of spillage of blood or pus from one lung to the noninvolved one, broncho-pleural or broncho-cutaneous fistula, an opened conducting airway, disruption of bullae or cysts, any thoracic injury with tracheobronchial tree disruption causing pneumomediastinum, and massive bleeding of a lung.[1,10] One-lung ventilation allows adequate ventilation of the normal lung preventing the ventilation from escaping through the lees resistance way of the disrupted structure. Relative indications for OLV are to facilitate surgical exposure and dissection, and to reduce operative time

by collapsing the lung on the operative side.[11] Visualization in thoracoscopic procedures is considerably aided by collapsing and immobilizing the operative lung, which helps to avoid excessive handling, compression and retraction.[1] This is important because trauma to the lung caused by retraction during surgery may impair gas exchange not only intraoperatively,[12-14] but also postoperatively.[15,16]

One-lung ventilation is the standard technique for thoracoscopic procedures in humans[17,18] and has been used in dogs as well.[19-22] Decreased pain, healing time and postoperative complications are some of the benefits justifying the increasing use of this minimally invasive surgery.[22,23]

Thoracoscopy can also be performed with CO_2 insufflation[24] but OLV is superior in terms of surgical visibility and hemodynamic stability, compared with insufflation with CO_2.[25] Carbon dioxide insufflation induces profound cardiovascular compromise with decreases in CO and SAP, and increase in CVP.[22,24]

B. WAYS TO ACHIEVE OLV.

Double-lumen endotracheal tubes, bronchial blockers and endobronchial tubes can be used to achieve OLV.[1] Endobronchial tubes are not commonly used.[1]

The double-lumen catheter was originally constructed in 1949 by Carlens for bronchospirometry but was adopted for endobronchial anesthesia.[26] It allowed anesthesia and suction to be applied to each lung separately, and resulted in a deflated lung that provided a greater operating space.[9,27] Double-lumen tubes are currently used for the majority of procedures in humans.[1]

The main advantage of DLT is the ability to perform independent bilateral suctioning to apply continuous positive airway pressure to the nonventilated lung if

necessary. With DLT it is easier to convert from TLV to OLV and vice versa. Double lumen tubes also allow specialized functions such as providing postoperative independent lung ventilation.[28] The disadvantages include the following: it cannot be used if the anatomy of the tracheobronchial tree is distorted, it needs to be changed to a single lumen tube at the end of the intervention, and it causes an increase in airway resistance.[1]

Lung isolation can also be achieved by passing a bronchial blocker through a single lumen endotracheal tube to occlude a main bronchus. This technique is mostly used in patients with narrowed or distorted airways. Embolectomy catheters (Fogarty catheters), pulmonary artery catheters and urinary catheters have been used as bronchial blockers.[29,30] The use of bronchial blockers such as the Univent tube, or other independently passed bronchial blockers, is increasing.[1]

The Univent tube is an endotracheal tube with a movable bronchial blocker.[31] The Univent tube was designed as an alternative to DLT. It is a conventional single lumen tube with an additional small channel within the concave anterior wall portion that houses a movable bronchial blocker used for lung isolation. The blocker can be advanced beyond the tip of the tracheal tube to occlude a main stem bronchus in order to isolate that lung.[32]

Univent tubes combine the advantages of DLT with the use of single-lumen endotracheal tubes with separate endobronchial blocking catheters. The Univent blocker's shaft is attached to the main tube so displacement is less likely to occur than with the use of the separate endobronchial blocking devices. In addition, a thin lumen in the blocker itself allows lung deflation, irrigation, suction, and various ventilatory interventions such as oxygen insufflation, continuous positive airway pressure, and high frequency ventilation.[28,32] Other advantages of the Univent tube are the possibility of

prolonged intubation without tube exchange, ability for selective blockade of lung segments, and ease of use.[28] Disadvantages of Univent tubes are their relatively large external diameter and the low-volume high-pressure cuff in the blocker.[30]

Main indications for the Univent tube include difficult intubation and planned postoperative ventilation.[32] It also seems to be one of the most effective and safest ways of achieving OLV in patients with narrowing of airways,[29] however, devices like wire-guided endobronchial blockers can be applied in morbidly obese, mouth opening-limited or critically ill patients where DLT or Univent tubes cannot be used.[33]

The use of a fiberoptic bronchoscope is required to confirm bronchial blockade with DLT and bronchial blockers.[30,32] Both DLT[34-36] and bronchial blockers[37] have been used in dogs.

C. DISTRIBUTION OF VENTILATION AND PERFUSION DURING OLV

The distribution of blood flow in the human lung is gravity dependent. In the upright position, blood flow decreases from dependent to nondependent lung areas, with very low values at the apex, which can be explained by the hydrostatic pressure differences within the blood vessels. In contrast, the alveolar pressure is equal throughout the lung. The alveoli at the apex of the lung are less compliant because they are distended due to the negative intrapleural pressure while the alveoli at the dependent part of the lung are less distended but more compliant.[38,39] Thus, a bigger proportion of the V_T is distributed to the more compliant regions at the base of the lung where perfusion is also favored, resulting in good V/Q matching preferentially in the dependent areas of the lung.[40-43]

In humans, pulmonary surgery is usually performed not with the patient upright but in the lateral decubitus position.[39] In this position the blood flow distribution is also gravity-dependent with a greater amount of blood going to the dependent lung compared to the nondependent lung.[39] If the patient is awake there is a good V/Q matching, and Q_S/Q_T is not affected significantly[39] because active contraction of the diaphragm directs ventilation preferentially to the dependent lung.[40] This is different in the anesthetized patient in the lateral position because as a result of general anesthesia and paralysis, the function of the diaphragm changes from its active contraction with spontaneous breathing, to a passive displacement of its upper part with the use of positive pressure ventilation, switching ventilation preferentially to the nondependent lung.[44] General anesthesia reduces FRC, and in the lateral position this effect is more pronounced on the dependent lung as a result of loss of lung volume, shifted mediastinum impeding expansion of the dependent lung, and pressure of abdominal contents.[1,39,45,46]

General anesthesia has an important effect on ventilation with the nondependent lung receiving ventilation in excess of perfusion.[44,47,48] Thus, with the dependent lung receiving more perfusion than the nondependent lung, general anesthesia with the patient in the lateral decubitus position results in V/Q mismatch and increase in Q_S/Q_T.[39]

With OLV, absorption atelectasis of the nondependent, nonventilated lung occurs after occlusion of its main bronchus,[49] and the V_T that was being used for two lungs is delivered to a single lung, increasing V/Q in the dependent, ventilated lung.[39] For OLV it has been recommended to ventilate the dependent lung with a V_T similar to that used during TLV to ventilate both lungs, and the respiratory rate to be adjusted to get a $PaCO_2$ around 40 mm Hg.[1] Thus, when OLV is started, the nondependent lung that had most of the ventilation, poorer perfusion and a high V/Q during TLV is now collapsed, and the

ventilation is redistributed to the dependent lung that had a better perfusion but poorer ventilation during TLV. Consequently, the decreased FRC of the dependent lung during TLV is relatively improved during OLV with this redistribution of the ventilation going to the better perfused, dependent lung.

D. CARDIOPULMONARY PARAMETERS DURING OLV

Arterial oxygen partial pressure and SaO_2 have been shown to decrease and Q_S/Q_T to increase, during OLV.[1,11,39,50,51] These changes are reversible and return to baseline values immediately when OLV is stopped.[52,53] One-lung ventilation results in a much larger P_A-aO_2 than during TLV.[11] Cardiac output is usually not altered during OLV[54] and pulmonary artery pressure increases.[50,54-56] Equilibration of respiratory parameters and Q_S/Q_T most likely occurs after 15 minutes of OLV in patients undergoing thoracic procedures.[55-57]

One-lung ventilation has been used safely in many interventions without cardiopulmonary complications. However, it has been reported that in some patients, severe hypoxemia may develop with PaO_2 values lower than 100 mm Hg,[52,58] and even lower than 70 mm Hg.[59]

E. SHUNT FRACTION DURING OLV

During OLV, the distribution of perfusion is the major determinant of the degree of shunt.[11] With the nondependent lung not receiving ventilation during OLV, blood flow through this lung constitutes an obligatory right-to-left shunt.[39,60] Studies during OLV have shown values of Q_S/Q_T ranging from 30%[13,50,51,61,62] to 44%.[52,57,59,63-65] Some of

these variations may be related to the position of the patient (right versus left lateral decubitus), given that the distribution of blood flow partially depends on the side of the thoracotomy.[40,43] Left thoracotomy is associated with a better PaO_2 during OLV than right thoracotomy, because the left lung normally receives 10% less CO than the right lung.[66] However, to estimate the amount of Qs/Qt during OLV with the patient in lateral position, on average it is considered that 40% of the CO goes to the nondependent lung and 60% goes to the dependent lung.[1] Shunt fraction is also inversely related to the amount of disease in the nondependent lung,[67,68] which also may account for some of the variations in the amount of shunt reported during OLV.

F. HYPOXIC PULMONARY VASOCONSTRICTION

Factors decreasing blood flow to the nondependent lung during OLV include passive mechanisms such as gravity, surgical manipulation, and pre-existing lung disease, or active mechanisms like HPV.[1]

Hypoxic pulmonary vasoconstriction was first demonstrated by Von Euler in 1946.[69] It is an autoregulatory mechanism that minimizes Qs/Qt by decreasing the amount of blood flow through the hypoxic lung.[1] During OLV, the normal response of the nonventilated, atelectatic lung is an increase in PVR[49,70,71] that diverts blood from the atelectatic lung toward the ventilated lung. During OLV, HPV normally should reduce blood flow to the nonventilated lung by about 50%;[60] the pulmonary vasculature constricts in response to alveolar hypoxia diverting blood flow away from hypoxic areas and increasing pulmonary artery pressure. This response is continuous and depends on the proportion of the lung that is hypoxic.[60]

Initial investigations established a relationship between alveolar oxygen tension and HPV.[72-75] Later works demonstrated that the HPV response to alveolar hypoxia is influenced also by PvO_2.[76-80]

One-lung ventilation causes hypoxia in 30-70 % of the lung mass, in this range, there is a large difference between the PaO_2 expected with normal HPV and the PaO_2 without HPV.[1]

Hypoxic pulmonary vasoconstriction produces the same percent of decrease in blood flow whether the chest is closed or open.[70]

1. Non-anesthetic factors affecting HPV

In early studies of OLV, it was assumed that HPV would be effective only after many hours had elapsed.[9] In more recent studies, HPV has been shown to be maximal after 15 minutes in dogs[81] and humans[82] undergoing unilateral hypoxic ventilation. These results agree with other studies in animals.[11]

It has been stated that HPV is enhanced with time,[83] however, there is a wide variation in reports concerning the time course of HPV with contradictory results.[81-85] In one study[83] it was shown that intermittent hypoxic challenges potentiates HPV. However, in this study an excess of manipulation and instrumentation may have interfered with the response. Compression and manipulation of the nonventilated lung may mechanically divert blood away from the nonventilated lung. This effect may appear as an enhancement of the HPV response with time decreasing shunt, but the extent of this effect is difficult to determine.[85] A study done in dogs showed that the HPV response was rapid in onset, sustained, and unchanged over 4 hours.[81] Inconsistencies in time course and stability of HPV, may be related to factors such as the use of excised lobes

preparations, dogs with whole lung hypoxia, in vitro pigs' lungs, or complications such as alkalosis, severe systemic hypoxemia, excessive sympathetic activity, respiratory alkalosis, low PvO_2 and increased CO.

The HPV response is maximal when PvO_2 is normal and is decreased by high or low values of PvO_2. Because alveolar and capillary oxygen partial pressures equilibrate by diffusion, low PvO_2 lowers PAO_2 in the ventilated lung producing a competing HPV that diverts blood away from the ventilated lung, and high PvO_2 increases PAO_2 in the nonventilated lung inhibiting HPV.[1,11]

Normocarbia has the least influence on HPV when compared with hypercapnia and hypocapnia.[39] It has been suggested that hypercapnia directly enhances HPV,[86-88] on the other hand it has been stated that hypercapnia during OLV has a selective vasoconstrictive effect on the ventilated lung increasing its PVR and diverting blood flow from the ventilated to the atelectatic lung.[39,89,90] Hypocarbia impairs HPV in the nonventilated lung.[89,90]

Acidosis increases HPV and alkalosis decreases it.[90] Variations in CO can affect HPV through pulmonary arterial pressure[91] having a passive effect on vascular caliber.[92]

Hypoxic pulmonary vasoconstriction is at its maximum with normal pulmonary arterial pressures. High or low pulmonary arterial pressures reduce HPV. The poor amount of pulmonary vascular smooth muscle cannot constrict against increased pulmonary arterial pressure, which counteracts HPV in the nonventilated lung.[91] With low pulmonary vascular pressure, PVR increases in the ventilated lung because the alveolar pressure increases in relation with the capillary pressure; increased PVR in the ventilated lung sends back blood flow to the nonventilated lung.[93]

Application of PEEP to the ventilated lung may increase regional PVR, diverting blood back to the nonventilated lung and having a counteracting effect on HPV.[1,34,94]

Vasoconstrictor drugs constrict the ventilated lung preferentially, increasing its vascular resistance and diverting blood back to the nonventilated lung.[95] However, the effect of dopamine on HPV varies with dose. It depresses HPV in dogs at a dose of 25 μg/kg/min but not at 2.5 μg/kg/min.[95] In humans, 5 μg/kg/min was found not to affect oxygenation during OLV.[85,96] Thus, dopamine appears to be a reasonable choice as a cardiovascular stimulant if needed during OLV.[1]

Nitric oxide is a potent vasodilator of vascular smooth muscle. Inhaled nitric oxide has a major influence on the pulmonary circulation and HPV, selectively decreasing PVR and dilating pulmonary vessels. When used during OLV, it has a vasodilating effect on the ventilated lung but because of its extremely short half life, it does not affect either systemic circulation or the nonventilated lung.[39] Other vasodilator drugs have been shown to inhibit HPV.[1]

2. Effects of anesthesia on HPV.

Inhaled anesthetics like isoflurane[97-99] and enflurane[71,97,100,101] have been shown to decrease the response of HPV. Many of these studies have been done using preparations in vitro. However, in intact animal preparations, some biologic or physiologic properties seem to remove or greatly lessen the inhibitory effect of anesthetic drugs on HPV.[1]

Isoflurane inhibits HPV in a dose dependent manner. Administration of 1 MAC of isoflurane anesthesia should cause a 21% decrease in the HPV response[102] resulting in only a 4% increase in Q_S/Q_T, and causing only slight impairment of arterial oxygenation during OLV.[57,103,104] Thus, 1 MAC of isoflurane anesthesia in patients with a moderate

level of shunting does not inhibit HPV enough to cause a significant decrease in PaO_2 during OLV in the lateral decubitus position. The magnitude of the HPV response was not altered during either sevoflurane or desflurane anesthesia.[105] In general, the contribution of volatile anesthetics to arterial hypoxemia during OLV is relatively minor,[56,57] and none of the injectable anesthetics have an effect on HPV.[98,106-109]

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CHAPTER III

POSITIVE END-EXPIRATORY PRESSURE REVIEW

A. INTRODUCTION

Positive end-expiratory pressure was first described in 1965.[1] It is a procedure used to oppose the tendency for lung atelectasis by keeping airway and alveolar pressures positive at the end of expiration.[2,3] With PEEP, instead of the alveoli returning to atmospheric pressure at the end of expiration, exhalation ends when alveolar pressure reaches the level of PEEP that is applied, with a consequent increase in FRC (the amount of gas that remains in the lung after expiration).[1] This increase in FRC decreases airway resistance and moves the lung higher on the pressure-volume curve, making more compliant those areas of the lung that were working less efficiently on the flat area of the curve as a result of their decreased volume.[1] With the lung working in a steeper area of the pressure-volume curve, ventilation is more efficient, given that less pressure is necessary to produce changes in volume.[3]

B. EFFECT OF PEEP ON PVR

Pulmonary vascular resistance is affected by the degree of inflation of the lungs; it is at its minimum when the lung volume is at FRC,[4] and it is increased when lung volume is either increased or decreased from FRC.[2,5-7] Positive end-expiratory pressure has been

shown to affect PVR because of modification of FRC.[8,9] The volume of the lung and the alveoli influences PVR because it alters the transmural pressure at the level of the capillaries.[7] Thus, if the alveoli are collapsed, PVR increases, and if the alveoli are then re-expanded with PEEP, the expanded alveoli exert traction on the capillary wall to open the capillary, thereby decreasing PVR. If, however, the alveoli are over-expanded with excessive amounts of PEEP, transmural pressure increases and collapses the capillaries resulting in a rise in the pulmonary arterial pressure.

C. EFFECT OF PEEP ON INTRAPLEURAL PRESSURE AND CO: CLOSED VERSUS OPEN CHEST

Cardiac output is determined by HR and stroke volume; and stroke volume depends on preload, afterload and contractility.[10] It is well established that PEEP can cause a reduction in CO.[11-17] The exact mechanism for this effect is controversial, but significant adverse hemodynamic effects generally occur.[1,12,14,17-21]

Possible mechanisms of reduced CO due to PEEP include a reduction in venous return,[11] decreased left and right ventricular preload,[14] increased right ventricular afterload,[4,5,14] leftward displacement of the interventricular septum,[15] obstruction of the right atrial filling by the rise of intrapleural pressure,[1] and a lung stretch depressor reflex releasing negative inotropic substances.[18]

Heart rate is not affected by the application of PEEP or by opening the thoracic cavity.[22] Contractility is not directly affected by PEEP either, instead, any variation in contractility with PEEP is associated with changes in preload.[23] During diastole, the main factors affecting preload are compliance and venous return. Intrathoracic pressure influences the pressure gradient necessary for blood to flow from the abdomen and

venous return to the thorax, which determines the actual amount of blood available to fill the ventricle.[14] An increase in intrathoracic pressure affects ventricular distensibility or compliance as well,[14] and may induce changes in the transmural pressure of the heart affecting afterload.[24] Afterload has also been shown to be affected by PEEP through increases in PVR.[5]

Intrathoracic pressure is an important factor related to venous return,[11] and appears to be an important part of the mechanisms involved in the decrease in CO with PEEP.[1,11,14,15]

Positive end-expiratory pressure increases intrapleural pressure, but by an amount much less than the PEEP that has been applied.[1] More than half of the pressure resulting from the use of PEEP is absorbed by the pulmonary transmural pressure, which increases along with PEEP. Increase in intrapleural pressure as a result of PEEP is more pronounced in less compliant lungs, thus, the greater the compliance, the smaller the increase in intrapleural pressure.[1]

In a normal lung, there is an intrapleural pressure of – 5 cm H_2O at the end of expiration.[25] In a hypothetical estimation based on the above mentioned values, if the proportion of PEEP transmitted to the intrapleural pressure is 40%, then the use of $PEEP_5$ would result in an increase of 2 cm H_2O in the intrapleural pressure, with a net intrapleural pressure of – 3 cm H_2O in a closed chest. In this case, intrapleural pressure would still be negative relative to atmospheric pressure, and would probably carry a lesser detrimental effect on venous return than that of atmospheric pressure with an open chest. Using the same estimation, 10 cm H_2O of PEEP would bring intrathoracic pressure to -1 cm H_2O, and 15 cm H_2O of PEEP would result in higher than atmospheric intrathoracic pressure of 1 cm H_2O.

From this perspective, the effect of PEEP on intrapleural pressure with a closed chest appears to be less predictable than during open chest, because with a closed chest the net intrapleural pressure depends on the combination between individual variations in lung compliance, and the amount of PEEP that is applied. In an open chest situation, intrapleural pressure is replaced by atmospheric pressure, which stays unchanged despite the use of any amount of PEEP or differences in lung compliance.

With a closed chest, negative intrapleural pressure is mainly maintained by the interaction between the lung and the chest wall acting in opposite directions, with elastic recoil that is inward for the lung and outward for the chest wall.[3] It may be logical to assume that in an open chest situation where the outward elastic recoil of the chest wall is lost and the intrathoracic pressure equals atmospheric pressure, the effect of transmission of an increased airway pressure to the intrathoracic space with PEEP is abolished. Therefore the effect of PEEP on venous return is less pronounced when the chest is open, especially for higher levels of PEEP that would result in a positive, supra atmospheric intrapleural pressure if the chest wall were intact.

A considerable proportion of the negative effect of PEEP, however, appears to occur independently of the closed-open chest situation,[26-31] and there has been controversy about whether PEEP lowers CO only by reducing preload or by a combination of mechanisms.[23]

With a closed chest, there is a relationship between pericardial pressure and right atrial pressure, with both increasing linearly with PEEP.[32] This increase in pericardial pressure, however, does not seem to happen only with closed chest, and CO has been shown to decrease with both closed and open chest with PEEP.[30] This decrease in CO independent of the closed-open chest situation has been shown to be related to the

traction that the lungs exert over the pericardium.[23] In a study with open chest, PEEP decreased preload and altered the shape and compliance of the left ventricle with increased ventricular filling pressures if the pericardium were intact. With the pericardium removed, there were no changes in the filling pressures and the left ventricular compliance was affected by only a small degree. In the same study, decreased contractility was found to be dependent on the reduced preload with PEEP.[23] In a different study with open chest,[26] PEEP caused a rise in atrial and mediastinal (juxtacardiac) pressures that diminished stroke volume, this decrease was greatest when the distension of the lung was adjacent to the right heart, and the increase in right atrial pressure was more associated with a decreased stroke volume than was the increase in left atrial pressure. Other studies also have supported the conclusion that decreased CO with PEEP is related to a combination of decreased preload and increased juxtacardiac pressure, occurring either with closed or open chest.[27] With the chest opened, pericardial pressure was found to exceed atmospheric pressure when PEEP was applied due to mechanical interaction between the lung and heart, and pericardial traction,[28,29] but CO was maintained after the use of 15 cm H_2O of PEEP in piglets with the thoracic cavity open and the pericardium retracted.[31]

D. VARIABILITY IN THE EFFECT OF PEEP

It has been stated that there are differences in the effect of PEEP in patients with healthy lungs and with diseased lungs.[1] These differences seem to be related to the positive and negative effects of PEEP.[1,9,15,33,34]

With healthy lungs, the decrease in CO has been shown to be minimal with PEEP of less than 10 cm H_2O, but significant decreases occur when PEEP exceeds this

amount.[33] In patients with diseased lungs, there was variation in the "optimal PEEP" that did not affect CO, but CO was significantly decreased when the level of PEEP was higher than the optimal value.[15,34]

In a human study, the application of PEEP improved PaO_2 only in patients with a low PaO_2 (< 80 mm Hg), but not in patients with an initial PaO_2 greater than 80 mm Hg.[9] The proposed reason for this effect is that hypoxemic patients are more likely to have lung volumes below the FRC with increased PVR. With the use of PEEP under these conditions, lung volume approaches FRC, decreasing PVR and increasing the blood flow to the dependent lung as a result.[9,35] For this reason, despite the decreased FRC by anesthesia in healthy patients, the improvement in oxygenation by PEEP is not as dramatic as it is in diseased patients that have a substantially decreased FRC.[1]

E. PEEP AND OLV

Reduction in FRC, by factors such as anesthesia, position, and pathological conditions, may lead to airway closure and atelectasis, especially in the more dependent parts of the lung, with consequent hypoventilation and gas exchange impairment.[1] With the patient in lateral decubitus position for most thoracic procedures,[36] the dependent lung develops atelectatic areas not only as a result of anesthesia and compression from abdominal organs, but also from the effect of mechanical ventilation with a paralyzed diaphragm, which directs most of the ventilation to the nondependent lung.[11,36-38]

Selective ventilation of the dependent lung, OLV,[11] is the most common technique during minimally invasive thoracic procedures.[11,39,40] With OLV the dependent lung receives the entire V_T that was used for TLV,[11] which may help to distend the alveoli that were previously collapsed during TLV.[36] However, there may still be areas of

patchy atelectasis of the dependent lung and hypoxemia with values of PaO_2 of less than 100 mm Hg,[41,42] and a significant incidence of PaO_2 values of less than 70 mm Hg[43] remains as a problem in many patients during OLV.[44,45] With OLV, there is also an increase in airway resistance because of the reduction of the tube diameter and decrease in compliance due to the reduction of the total ventilated lung mass.[46]

With OLV, an increased Q_S/Q_T causes decreases in PaO_2 and SaO_2.[11,36,47,48] This increased Q_S/Q_T during OLV is related to the continuing blood flow going to the nonventilated lung despite HPV, and it is also related to the amount of blood circulating through atelectatic areas in the ventilated lung.[11,36] Therefore, any maneuver applied to the ventilated lung to improve its gas exchange capability may contribute to a decrease in Q_S/Q_T and improve oxygenation during OLV.

Shortly after OLV was used for the first time in 1931, some reports recommended "inflation of the atelectatic lung for short periods at intervals when necessary" given that some patients showed a decreased saturation and pronounced cyanosis. An increase in the pressure of the inspiratory phase also was often found necessary owing to the increased resistance created by the smaller lumen of the tube.[49,50]

Pharmacologic treatments such as nitric oxide,[51] prostaglandin E_1,[52] and the use of different anesthetic drugs,[47,48,53-55] have been used to prevent hypoxemia during OLV, but they do not improve oxygenation consistently, and hypoxemia can remain a problem even with the use of high inspired fractions of oxygen.[43,56] Use of a high concentration of oxygen,[43,56] the application of continuous positive airway pressure to the nonventilated lung,[57] increase in V_T,[35] and application of PEEP to the dependent or nondependent lung,[8,35,58] have also been used to prevent hypoxemia during OLV with variable results.

Continuous positive airway pressure consists of a breathing circuit that keeps pressure above atmospheric at all times.[1] Selective continuous airway pressure to the nonventilated lung[59] does not produce consistent satisfactory effect on oxygenation.[60,61]

Positive end-expiratory pressure has been used as a rapid method to improve oxygenation.[1,37,46,62,63] However, the use of PEEP in the dependent ventilated lung during OLV carries the risk of volume-induced compression of intra-alveolar vessels if there is excessive airway pressure, increasing PVR which diverts blood away from the ventilated lung, resulting in increased Qs/Qt and decreased oxygenation.[11,58,59] Levels of PEEP less than 5 cm H_2O are unlikely to increase PVR while PEEP in excess of 5 cm H_2O has been shown to increase PVR in the ventilated lung.[64]

During OLV however, the well-known negative effect of PEEP decreasing CO is not as pronounced as it is during TLV.[26] There is a greater increase in juxtacardiac pressure and decrease in stroke volume with both lungs ventilated than when only upper lobes, lower lobes,[26] or the right and left lungs are selectively ventilated.[26,65] In addition, there is a difference in the degree of reduction in CO depending on which lung is receiving PEEP, with a greater increase in pericardial pressure and decrease in CO with PEEP on the right lung than with PEEP applied to the left lung. The mechanism involved in this variation is unknown but may be related to anatomic factors.[65]

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HYPOTHESIS

One-lung ventilation is the technique of choice for thoracic procedures. Hypoxemia as defined by PaO_2 < 70 mm Hg and SaO_2 < 94 %, is a common complication of OLV.

Oxygen delivery is a calculated parameter that integrates the respiratory and circulatory systems. Its calculation is based not only on PaO_2 and SaO_2 as the main determinants of CaO_2, but also on CO to estimate the actual amount of oxygen that is delivered to the tissues.

The impairment of oxygenation during OLV is due to an increased Q_S/Q_T caused by blood circulating through both, the nonventilated lung and atelectatic areas in the ventilated, dependent lung. Any maneuver addressed to improve gas exchange in the ventilated lung will potentially lead to better oxygenation during OLV.

Many techniques have been used to improve oxygenation during OLV, some of them however, have disadvantages such as impairing visibility, compromising the desired immobility of the surgical area, and reducing CO. Application of PEEP to the ventilated lung is used as a rapid method to improve oxygenation by increasing the resting lung volume at the end of expiration. It increases FRC contributing to recruitment of alveoli, preventing airway closure and improving ventilation and gas exchange in atelectatic areas. Positive end-expiratory pressure applied to the ventilated lung does not produce impairment in visibility or immobility; its use, however, has been associated with a

decrease in CO. Therefore, improvement in oxygenation with PEEP during OLV depends on the balance between the improvement in gas exchange, and a possible PEEP-induced decrease in CO.

Positive end-expiratory pressure produces an increase in intrathoracic pressure proportional to the amount of PEEP that is being used, decreasing venous return and CO. The negative effect of PEEP depends in part on the amount of PEEP that is being used. It has been proved that high levels of PEEP such as 10 cm H_2O produce negative effects on CO. This effect takes place when the thoracic cavity is closed. If during OLV, PEEP is applied only to the ventilated lung, absorption atelectasis of the nonventilated lung should allow expansion of the ventilated lung and limit the augmentation of intrathoracic pressure. Therefore, PEEP during OLV in a closed chest situation likely will have a less negative effect on hemodynamic parameters compared to PEEP applied during TLV in a closed chest situation.

Despite the variations in intrathoracic pressure affecting venous return and CO with a closed chest, an important part of the negative effect of PEEP has been proved to happen independently of the closed-open chest situation. Thus, there is an anatomic component associated with traction of the pericardium resulting in increased atrial pressures and possibly an interactive effect taking place depending on the chest being closed or open to determine differences in the behavior of OLV and PEEP with closed and open chest.

Calculation of DO_2 during OLV will lead to more precise information about the effect of OLV on the amount of oxygen that is available to the tissues. The questions to be answered then are: what is the response of DO_2 to OLV, what levels of PEEP would

influence this response, and are these responses the same whether the thoracic cavity is closed or open?

Our hypothesis is that OLV and PEEP during OLV will affect DO_2 with either a closed or an open chest situation in dogs.

CHAPTER IV

CARDIOPULMONARY EFFECTS OF ONE-LUNG VENTILATION IN ANESTHETIZED DOGS WITH A CLOSED THORACIC CAVITY

A. INTRODUCTION AND HYPOTHESIS

One-lung ventilation is the isolation and selective ventilation of one lung.[1] Absolute indications for the use of OLV include an infected or purulent lung, a bronchopleural or bronchocutaneous fistula, or an open conducting airway. One-lung ventilation is also indicated for the control of pneumothorax caused by the disruption of bullae or cysts. Thoracic injury with disruption of the tracheobronchial tree resulting in pneumomediastinum or massive bleeding of a lung may require OLV to protect and allow adequate ventilation of the remaining normal lung.[1-3] In those situations, use of OLV with a closed thoracic cavity becomes a mandatory lifesaving maneuver to gain time and to allow better ventilation before thoracic surgical procedures are performed.[3]

Double-lumen tubes, endobronchial intubation, and bronchial blockade have been used to achieve OLV.[4] Many studies[5-7] have documented that conversion from TLV to OLV causes significant decreases in PaO_2 and SaO_2, and a significant increase in Q_S/Q_T.

Delivery of oxygen requires integration of the respiratory, cardiovascular, and microvascular systems.[8] It is a function of CO and CaO_2.[9] The ultimate goal during provision of critical care is to optimize DO_2 to vital organs and peripheral tissues. The effect of OLV on DO_2 has been assessed in a limited number of studies.[6,10]

Hemodynamic and pulmonary variables have been studied separately but have not been integrated to calculate DO_2.[5,11] To the author's knowledge, the net effect of OLV on DO_2 has not been evaluated in situations involving a closed thoracic cavity. Therefore, the purpose of the study reported here was to describe the respiratory and hemodynamic changes induced by use of OLV in anesthetized dogs with a closed thoracic cavity, and to calculate DO_2 as a more accurate assessment of the actual availability of oxygen to tissues. We hypothesized that OLV would affect DO_2 in dogs with a closed thoracic cavity.

B. MATERIALS AND METHODS

Animals

Seven healthy dogs, as determined on the basis of results of physical and hematologic examinations, were included in the study. Dogs were of both sexes, and each weighed between 25 and 30 kg and was between 2 and 5 years old. Food was withheld from each dog beginning 12 hours before the onset of the study. The study was approved by the Colorado State University Animal Care and Use Committee. Dogs were adopted at the end of the study.

Procedure

Each dog was its own control. The dogs received no medications prior to induction of anesthesia. An 18-gauge over-the-needle catheter[a] was inserted in a cephalic

vein and a bolus of lactated Ringer's solution[b] (10 mL/kg) was administered IV. Induction of anesthesia was accomplished by IV administration of propofol[c] (3 to 4 mg/kg) and diazepam[d] (0.3 mg/kg). Endotracheal intubation was performed, and anesthesia was maintained with an end-tidal concentration of isoflurane[e] of 1.85% to 1.95% (approx 1.5 times the minimum alveolar concentration) in oxygen, delivered through a precision out-of-circuit vaporizer[f] in a semiclosed circle rebreathing system. An agent analyzer[g] was used to measure end-tidal isoflurane concentration. An esophageal temperature probe[h] was advanced to the region of the heart base to measure core body temperature. Maintenance fluids consisted of IV administration of lactated Ringer's solution[b] (5 mL/kg/h) and a solution of dextrans[i] (5 mL/kg/h). To facilitate intermittent positive-pressure ventilation, the dogs were administered a paralytic agent (atracurium[j]; 0.2 mg/kg, IV as a bolus, followed by 0.1 mg/kg IV, repeated as needed). A nerve stimulator[k] placed over the peroneal nerve was used to assess muscle relaxation by enabling investigators to observe the response to a train-of-four electrical stimulation.

The dogs were positioned in right lateral recumbency. A volume-limited ventilator[l] was adjusted to provide a baseline $PaCO_2$ of 35 to 45 mm Hg. End-tidal partial pressure of carbon dioxide was monitored by use of a side-stream capnograph[m] connected to the endotracheal tube. Once a $PaCO_2$ of 35 to 45 mm Hg was achieved and maintained, respiratory rate (7 to 16 breaths/min) and VT (14 to 15 mL/kg) were not changed during the remainder of the study. A respirometer[n] was used to measure expiratory VT.

Hemodynamic and cardiorespiratory variables

A 20-gauge over-the-needle catheter[a] was inserted in the dorsal pedal artery. Systolic arterial pressure, DAP, and MAP were recorded continuously on a pressure monitor.[o] Results of ECG and pulse oximetry[p] were also recorded on the monitor. A 7.5-F Swan-Ganz catheter[q] was inserted in the pulmonary artery through an 8-F introducer[r] that had been inserted in the jugular vein; characteristic waveforms were used to guide proper placement of the catheter in the pulmonary artery. Each catheter was connected to fluid-filled pressure transducers[s] and zeroed at the level of the right atrium.

Systolic pulmonary artery pressure, DPAP, and MPAP were also recorded continuously on a pressure monitor.[t] Pulmonary artery wedge pressure, RAP and HR were recorded. Cardiac output was measured by use of the thermodilution technique. Ten milliliters of ice-cold saline (0.9% NaCl) solution was injected into the right atrium, and the mean of 3 measurements was determined by the use of a CO computer.[u]

Blood gas analysis[v] was performed on heparinized blood samples. Arterial and mixed venous blood samples were collected via the catheters inserted in the pedal and pulmonary arteries respectively, and samples were analyzed immediately after collection to determine PaO_2, PvO_2, SaO_2, SvO_2, $PaCO_2$, pHa, HCO_3^-a, and ABEa.

Values were calculated for the following variables: $Cc'O_2$, P_AO_2, Q_S/Q_T, CaO_2, CvO_2, $P_{A-a}O_2$, DO_2, CI, O_{2ER}, PVRI, SVRI, and V_D/V_T. (See appendix for formulas).

Collection of data

Data was collected during TLV after the baseline $PaCO_2$ was stable for at least 15 minutes within the range of 35 to 45 mm Hg. The left bronchus of each dog was then obstructed by use of a bronchial blocker[w] inserted through a multiple-port airway

adapter[x] that had been attached into the endotracheal tube. Bronchoscopy[y] was used to ensure appropriate placement of the blocker and adequate obstruction of the bronchus. After the left bronchus was blocked, 15 minutes were allowed for equilibration, and data was then collected for the OLV period. Dogs were recovered in a critical care unit under standard care as for client owned animals.

Statistical analysis

An ANOVA for repeated measurements[12] with the Fisher's least significant difference test were used to statistically evaluate the effects of OLV on cardiopulmonary variables. Values of $P < 0.05$ were defined as significant. Data was reported as mean ± SE.

C. RESULTS

Results for respiratory, hemodynamic, and calculated cardiopulmonary variables for TLV and OLV are shown on tables 4.1, 4.2, and 4.3 respectively. One-lung ventilation induced a significant reduction in PaO_2 ($P < 0.001$) and SaO_2 ($P = 0.002$) and a significant increase in mean $PaCO_2$ ($P = 0.042$). Systolic arterial pressure, DAP and MAP were significantly increased by OLV ($P = 0.048$, $P = 0.034$, and $P = 0.026$ respectively). Systolic pulmonary artery pressure and MAP also were significantly increased after induction of OLV ($P = 0.002$, and $P = 0.004$ respectively)

One-lung ventilation induced a significant augmentation Qs/Q_T, $P_A\text{-}aO_2$ and V_D/V_T ($P = 0.002$, $P < 0.001$, and $P = 0.001$ respectively), and a significant reduction in CaO_2 ($P < 0.001$). However, CI ($P = 0.055$), SVRI ($P = 0.977$), and PVRI ($P = 0.928$) were not significantly affected by OLV. Similarly, DO_2 did not change significantly ($P = 0.129$) during OLV.

D. DISCUSSION

One-lung ventilation in clinically normal dogs with a closed thoracic cavity did not significantly affect DO_2 despite a decrease in PaO_2 and augmentation of $\dot{Q}S/\dot{Q}T$. One-lung ventilation induced a reduction in PaO_2 and SaO_2, however, it resulted in only a small reduction of CaO_2. Because CI was not significantly changed, DO_2 was not significantly affected by OLV. Similar results have been documented in human patients during thoracic surgery.[6,10]

Adequate oxygenation of peripheral tissues is a balance between delivery and the metabolic demands of the tissue. The O_{2ER} is another variable that indicates the balance between DO_2 and oxygen demand. An increase in O_{2ER} is an indication of reduction of DO_2 or an increase in oxygen demand.[8] Because the dogs reported here were anesthetized and their core body temperature did not change during the experiment, we can assume that the metabolic demand of the tissues during this experiment did not change. Therefore, because the O_{2ER} was not significantly altered in this study, it confirms that DO_2 was not significantly affected by OLV.

Arterial oxygen content is a function of PaO_2, SaO_2, and Hb concentration. In the study reported here, although the decrease in PaO_2 was statistically significant, the reductions in SaO_2 and CaO_2 were not biologically important because of the shape of the oxygen-dissociation curve. At baseline, SaO_2 was > 92%, which falls on the flat portion at the top of the oxyhemoglobin dissociation curve. Therefore, the variation in PaO_2 recorded in this study could only have a minimal effect on SaO_2 and CaO_2[13] Patients with compromised lung function resulting from pneumothorax or lung disease may have a more important clinical response because the baseline SaO_2 with TLV will be lower. One-lung ventilation may induce substantial desaturation in those patients.

Atelectasis of the nonventilated lung was expected after occlusion of its main bronchus because absorption atelectasis can develop in < 6 minutes in patients breathing 100% oxygen.[14,15] Atelectasis induced an increase in Q_S/Q_T, and P_A-aO_2. The passive effect of gravity on the pulmonary circulation tends to reduce the amount of shunting during OLV when the ventilated lung is the dependent lung. However, in the study reported here with the dogs positioned in right lateral recumbency, the dependent ventilated lung most likely developed areas of atelectasis, which also contributed to the augmentation of pulmonary shunting.

Hypoxic pulmonary vasoconstriction is an active vasoconstrictor mechanism that redistributes blood flow away from nonventilated alveoli to ventilated alveoli.[16-20] During OLV, the amount of shunting is decreased by HPV.[21] Response to HPV in dogs is predictable and continuous depending on the size of the hypoxic segment and F_IO_2.[22] It has been reported[23] that HPV can induce a 58% reduction of blood flow in a hypoxemic lung. However, HPV can be inhibited by a number of factors, including high or low pulmonary vascular pressure,[17,18,24] high or low PvO_2,[25,26] hypocapnia,[17,27] vasodilating agents,[28,29] vasoconstricting agents,[30,31] and anesthetic agents.[5,22] Isoflurane was used during our study, and it may have substantially reduced the HPV response to hypoxemia, which resulted in major shunting of blood in the nonventilated lung. Isoflurane induces a reduction of HPV in a dose-dependent manner.[32] The plane of anesthesia was not modified during this study; therefore, we can expect that the HPV effect was not different between the TLV and OLV situations. Because PVR was not significantly affected in this study, we can assume that HPV was obtunded by the isoflurane and a substantial amount of blood was still shunting in the nonventilated lung. Isoflurane was used because it is an

anesthetic that is commonly used in clinical settings.[33] Similar effects have been reported[5,11] for sevoflurane.

Pulmonary vascular resistance is a function of CO, MPAP, and PAWP.[13,34] In the study reported here, MPAP increased significantly during OLV whereas CI and PAWP increased but not significantly. The net effect was a nonsignificant augmentation of the calculated PVRI, as determined in accordance with the standard equation derived from Ohm's law (see appendix for equation). Transmural pressure at the level of the capillaries,[35-37] the recruitment of capillaries with increases in CO,[38,39] and hypoxemic vasoconstriction[16-19] are important variables that will affect PVR. Hypoxemic pulmonary vasoconstriction was probably abolished in this study by the use of isoflurane.[1,5,11] More likely, transmural pressure was increased in our study because the entire TLV volume was redistributed during OLV to 1 lung. Augmentation of MPAP was a reflection of augmentation of the transmural pressure. However, this augmentation did not translate into an augmentation of PVRI because the PWAP also increased during the study. Augmentation of PWAP was not significant; however, it was sufficient to prevent a significant augmentation of the PVRI. It was beyond the scope of this study to evaluate the physiologic characteristics of pulmonary circulation during OLV in dogs. Distribution of colored microspheres injected in the pulmonary artery would be required to evaluate distribution of blood flow in the pulmonary parenchyma after institution of OLV.

Physiologic dead space increased with OLV in the study reported here, but it remained within the reference range. Physiologic dead space is typically 20% to 35% during breathing in resting humans and resting unsedated tracheostomized dogs.[33,40] During OLV, a high V/Q ratio is created in the ventilated lung because the V_T that was being used for 2 lungs now is delivered to only a single lung. Ventilated alveoli then

receive excess ventilation that is defined as wasted ventilation, which results in an augmentation of dead space documented by the augmentation of V_D/V_T.[41] Wasted ventilation results in dilution of the CO_2 that enters the alveoli, and $P_{ET}CO_2$ is consequently reduced to a lower value than $PaCO_2$.[42] We could have changed the V_T of the ventilator to reduce the wasted ventilation; however, doing so may have had an impact on the depth of anesthesia and SaO_2, which would have added another variable to our study.

In the study reported here, $PaCO_2$ increased significantly; however, OLV is typically expected to have a less dramatic impact on $PaCO_2$ than on PaO_2[1] because of the differing physiologic behaviors of the two gases.[43] The arterial-venous gradient of carbon dioxide is small, and carbon dioxide is approximately 20 times more soluble than oxygen.[43] The carbon dioxide dissociation curve is steeper than the oxygen-dissociation curve, with no steep or flat portions (nearly a straight line). Therefore, there is a greater change in arterial CO_2 content per change in $PaCO_2$ than there is in CaO_2 per change in PaO_2.[43] Thus, the net effect during OLV is that the ventilated lung with a high V/Q ratio cannot compensate for the nonventilated lung with a low V/Q ratio, which results in relative hypoxemia and a more modest hypercapnia.[13]

In the study reported here, the use of a paralytic drug was indicated to facilitate use of mechanical ventilation.[44] Some neuromuscular blockers can release histamine, which can induce effects on the cardiovascular system,[44] such as hypotension.[45] However, the amount of histamine released in dogs by the use of atracurium is insubstantial at the doses used for neuromuscular blockade, and hypotension would develop only at supramaximal doses.[45] None of the dogs had hypotension at any point in our study.

One limitation of the study was that it was performed on healthy dogs with normal gas exchange. Patients with compromised cardiopulmonary function may have differing reactions to OLV, compared with results for clinically normal dogs.

A second limitation of the study was that the order of the treatments (TLV and OLV) was not randomized. Some variations in cardiopulmonary variables may develop over time[7]; however, besides the short period used to insert the bronchoscope and the bronchial blocker, there was an interval of only 15 minutes between data collection for TLV and OLV, as has been recommended in most research protocols that involve measurement of the impact of treatment on hemodynamic variables. Therefore, it is unlikely that the changes observed in the study were related to time.

Another limitation was the relatively small number of dogs used in the study. This results in a low power. However, we have great confidence in our results because OLV induced only minimal changes in the data we collected. Oxygen content decreased by 4% and DO_2 increased nonsignificantly by 17%. Thus, DO_2 tended to increase, not decrease as expected.

Analysis of the results of the study reported here suggests that the use of OLV in healthy dogs for the conditions described did not cause a negative effect on tissue oxygenation. Therefore, OLV can be used in patients that are hemodynamically stable because it will not induce a reduction of DO_2. However, additional studies are necessary to evaluate OLV in diseased patients and for various conditions of age and body position.

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Table 4.1 Mean ± SE values for respiratory variables of 7 clinically normal anesthetized dogs during TLV followed by OLV.

Variable*	TLV	OLV	*P*-value**	Power
PaO_2 (mm Hg)	448 ± 24	170 ± 25	< 0.001	NA
$PaCO_2$ (mm Hg)	40 ± 1	44 ± 2	0.042	NA
PvO_2 (mm Hg)	68 ± 3	60 ± 3	0.102	0.113
pHa	7.35 ± 0.01	7.30 ± 0.02	0.028	NA
HCO_3^-a (mEq/L)	22.0 ± 0.5	22.0 ± 0.4	0.252	0.269
ABEa (mEq/L)	–4.0 ± 0.5	–4.1 ± 0.6	0.700	0.710
$P_{ET}CO_2$ (mm Hg)	35 ± 1	35 ± 2	0.834	0.840
SaO_2 (%)	99.90 ± 0.02	98.60 ± 0.24	0.002	NA
SvO_2 (%)	87.3 ± 3.7	86.4 ± 1.3	0.819	0.825

* See list of abbreviations. ** Analysis of general effect; significance was defined as values of $P < 0.05$. NA = Not applicable.

Table 4.2 Mean ± SE values for hemodynamic variables of 7 clinically normal anesthetized dogs during TLV followed by OLV.

Variable*	TLV	OLV	*P*-value**	Power
SAP (mm Hg)	95 ± 5	108 ± 6	0.048	NA
DAP (mm Hg)	50 ± 2	57 ± 3	0.034	NA
MAP (mm Hg)	64 ± 3	74 ± 3	0.026	NA
RAP (mm Hg)	5.0 ± 0.3	5.0 ± 0.3	0.355	0.374
PAWP (mm Hg)	6 ± 1	6 ± 1	0.482	0.498
SPAP (mm Hg)	19 ± 1	21 ± 1	0.002	NA
DPAP (mm Hg)	9 ± 1	11 ± 1	0.095	0.105
MPAP (mm Hg)	14 ± 1	16 ± 1	0.004	NA
HR (beats/min)	107 ± 5	117 ± 4	0.078	0.088
Core body temperature (^{o}C)	36.5 ± 0.3	36.5 ± 0.3	0.289	0.476
* See list of abbreviations. ** Analysis of general effect; significance was defined as values of $P < 0.05$. NA = Not applicable.				

Table 4.3 Mean ± SE values for calculated cardiopulmonary variables of 7 clinically normal anesthetized dogs during TLV followed by OLV.

Variable*	TLV	OLV	*P*-value**	Power
CaO_2 (mL/dL)	22.7 ± 0.8	21.6 ± 0.8	< 0.001	NA
Qs/Q_T (%)	8 ± 1	30 ± 2	0.002	NA
DO_2 (mL/kg/min)	876 ± 78	1,028 ± 136	0.129	0.142
PVRI (mm Hg/L/min/m^2)	2.0 ± 0.3	2.0 ± 0.2	0.928	0.931
SVRI (mm Hg/L/min/m^2)	15 ± 1	15 ± 2	0.977	0.978
O_{2ER} (%)	12.6 ± 0.4	12.4 ± 0.1	0.960	0.962
CI (L/min/m^2)	4.2 ± 0.4	5.1 ± 0.6	0.055	0.062
V_D/V_T (%)	12 ± 3	21 ± 2	0.001	NA
P_A-aO_2 (mm Hg)	102 ± 20	375 ± 27	< 0.001	NA
PaO_2 (mm Hg)	551 ± 6	545 ± 6	0.042	NA
* See list of abbreviations. ** Analysis of general effect; significance was defined as values of $P < 0.05$. NA = Not applicable.				

CHAPTER V

CARDIOPULMONARY EFFECTS OF POSITIVE END-EXPIRATORY PRESSURE DURING ONE-LUNG VENTILATION IN ANESTHETIZED DOGS WITH A CLOSED THORACIC CAVITY

A. INTRODUCTION AND HYPOTHESIS

One-lung ventilation is the isolation and selective ventilation of one lung.[1] One-lung ventilation has primarily been used to facilitate thoracic surgery and minimally invasive surgery.[2] One-lung ventilation is typically initiated at the request of a surgeon once the thoracic cavity of the patient has been opened. Indications for starting OLV in patients with a closed thoracic cavity have been reported.[2,3] Absolute indications for the use of OLV include an infected lung, a bronchopleural or bronchocutaneous fistula, an opened conducting airway, bullae or cysts, any tracheobronchial disruption that may cause pneumomediastinum, and certain cases of pneumothorax and hemothorax after chest trauma.[1,2,4] In those situations, OLV is established in patients with a closed thoracic cavity as a maneuver to isolate injured areas of the lungs and to stabilize the patient before surgery is performed.

One-lung ventilation induces cardiopulmonary changes that result in a substantial augmentation of Q_S/Q_T, which in turn causes a substantial reduction in PaO_2 and alters

SaO_2.[5-7] Use of a high concentration of oxygen,[8,9] application of continuous positive airway pressure to the nonventilated lung,[10] an increase in V_T,[11] and application of PEEP to the dependent or nondependent lung[11-13] have been used to prevent or minimize hypoxemia during OLV. Positive end-expiratory pressure has been used to rapidly increase CaO_2 by increasing FRC, which contributes to recruitment of alveoli, and thus prevents airway closure and improves gas exchange.[14-16]

The amount of oxygen available for tissue metabolism is determined by the amount of oxygen delivered. Oxygen delivery is dependent on CO and CaO_2.[17,18] Use of high values of PEEP in patients with a closed thoracic cavity has been associated with a reduction in CO, which may decrease DO_2.[1,19,20]

The use of high levels of PEEP in the dependent, ventilated lung during OLV carries the risk of volume-induced compression of intra-alveolar vessels, which will increase PVR and thus divert blood away from the ventilated lung, increasing shunting and decreasing oxygenation.[1] Therefore, the net effect of PEEP on DO_2 may be compromised if there is a greater reduction in CO, compared with the degree of improvement in CaO_2.

The objective of the study reported here was to determine changes in hemodynamic and respiratory variables when PEEP was applied to the dependent lung during OLV in anesthetized dogs with a closed thoracic cavity.

We hypothesized that application of PEEP during OLV would affect DO_2 in clinically normal dogs.

B. MATERIALS AND METHODS

Animals

Seven healthy dogs, as determined on the basis of results of physical examination, a CBC count, and serum biochemical analysis, were included in the study. Dogs were sexually intact, of both sexes, and weighed between 25 and 30 kg. Dogs were between 2 and 5 years old. Food was withheld from each dog beginning 12 hours before the onset of the study. The study was approved by the Colorado State University Animal Care and Use Committee. Dogs were adopted at the end of the study.

Procedure

Each dog was its own control. The dogs received no medications prior to induction of anesthesia. An 18-gauge over-the-needle catheter[a] was inserted in a cephalic vein and a bolus of lactated Ringer's solution[b] (10 mL/kg) was administered IV. Induction of anesthesia was accomplished by IV administration of propofol[c] (3 to 4 mg/kg) and diazepam[d] (0.3 mg/kg). Endotracheal intubation was performed, and anesthesia was maintained with an end-tidal concentration of isoflurane[e] of 1.85% to 1.95% (approx 1.5 times the minimum alveolar concentration) in oxygen, delivered through a precision out-of-circuit vaporizer[f] in a semiclosed circle rebreathing system. An agent analyzer[g] was used to measure end-tidal isoflurane concentration. An esophageal temperature probe[h] was advanced to the region of the heart base to measure core body temperature. Maintenance fluids consisted of IV administration of lactated Ringer's solution[b] (5 mL/kg/h) and a solution of dextrans[i] (5 mL/kg/h). To facilitate intermittent positive-pressure ventilation, the dogs were administered a paralytic agent (atracurium[j]; 0.2 mg/kg, IV as a bolus, followed by 0.1 mg/kg IV, repeated as needed). A nerve

stimulator[k] placed over the peroneal nerve was used to assess muscle relaxation by enabling investigators to observe the response to a train-of-four electrical stimulation.

The dogs were positioned in right lateral recumbency. A volume-limited ventilator[l] was adjusted to provide a baseline $PaCO_2$ of 35 to 45 mm Hg. End-tidal partial pressure of carbon dioxide was monitored by use of a side-stream capnograph[m] connected to the endotracheal tube. Once a $PaCO_2$ of 35 to 45 mm Hg was achieved and maintained, respiratory rate (7 to 16 breaths/min) and VT (14 to 15 mL/kg) were not changed during the remainder of the study. A respirometer[n] was used to measure expiratory VT.

Hemodynamic and cardiorespiratory variables

A 20-gauge over-the-needle catheter[a] was inserted in the dorsal pedal artery. Systolic arterial pressure, DAP, and MAP were recorded continuously on a pressure monitor.[o] Results of ECG and pulse oximetry[p] were also recorded on the monitor. A 7.5-F Swan-Ganz catheter[q] was inserted in the pulmonary artery through an 8-F introducer[r] that had been inserted in the jugular vein; characteristic waveforms were used to guide proper placement of the catheter in the pulmonary artery. Each catheter was connected to fluid-filled pressure transducers[s] and zeroed at the level of the right atrium.

Systolic pulmonary artery pressure, DPAP, and MPAP were also recorded continuously on a pressure monitor.[t] Pulmonary artery wedge pressure, RAP and HR were recorded. Cardiac output was measured by use of the thermodilution technique. Ten milliliters of ice-cold saline (0.9% NaCl) solution was injected into the right atrium, and the mean of 3 measurements was determined by the use of a CO computer.[u]

Blood gas analysis[v] was performed on heparinized blood samples. Arterial and mixed venous blood samples were collected via the catheters inserted in the pedal and pulmonary arteries respectively, and samples were analyzed immediately after collection to determine PaO_2, PvO_2, SaO_2, SvO_2, $PaCO_2$, pHa, HCO_3^-a, and ABEa.

Values were calculated for the following variables: $Cc'O_2$, PAO_2, Q_S/Q_T, CaO_2, CvO_2, $PA\text{-}aO_2$, DO_2, CI, O_{2ER}, PVRI, SVRI, and V_D/V_T. (See appendix for formulas).

Collection of data

The left bronchus of each dog was obstructed by use of a bronchial blocker[w] inserted through a multiple port adapter[x] that had been attached into the endotracheal tube. Bronchoscopy[y] was used to ensure appropriate placement of the blocker and adequate obstruction of the bronchus. After the left bronchus was blocked, 15 minutes were allowed for equilibration, and data was then collected for the OLV period (baseline). Following these measurements, $PEEP_{2.5}$ was applied, a similar equilibration period was provided, and measurements were again obtained. Finally $PEEP_5$ was applied, a 15-minute equilibration period was provided, and measurements were recorded. Dogs were recovered in a critical care unit under standard care as for client owned animals.

Statistical analysis

An ANOVA for repeated measurements[21] was used to evaluate the effects of $PEEP_{2.5}$ and $PEEP_5$ on hemodynamic and respiratory variables during OLV. Data were reported as mean ± SE. Values of $P < 0.05$ were considered significant. When the P value was significant, comparisons were made among treatment groups by use of the Fisher's least significant difference test.

C. RESULTS

Results for respiratory, hemodynamic, and calculated cardiopulmonary variables for OLV with 0 PEEP, $PEEP_{2.5}$, and $PEEP_5$ are shown on tables 5.1, 5.2, and 5.3 respectively. During OLV, the use of $PEEP_5$ caused a significant ($P = 0.022$) augmentation of SaO_2. There were significant increases in RAP and PAWP ($P = 0.007$ and $P < 0.001$ respectively), and in SPAP, DPAP and MPAP ($P = 0.033$, $P = 0.049$ and $P < 0.011$ respectively).

Cardiac index was not significantly ($P = 0.416$) affected by the use of PEEP, which resulted in no variation of PVRI ($P = 0.141$). Furthermore, the significant increase of SaO_2 with $PEEP_5$ did not result in a significant ($P = 0.058$) augmentation of CaO_2. There was a significant ($P = 0.015$) reduction of Q_S/Q_T. The net effect of PEEP on hemodynamic and respiratory variables resulted in no significant change in DO_2 ($P = 0.472$).

D. DISCUSSION

Application of PEEP did not reduce CO during OLV in dogs with a closed thoracic cavity. Positive end-expiratory pressure reduced the amount of pulmonary shunting; however, CaO_2 did not improve significantly in the dogs in the study reported here. Therefore, DO_2 was not improved because CaO_2 was not increased by a clinically important amount. Oxygen content would most likely be improved in patients with pulmonary disease with reduced baseline SaO_2. Therefore, we recommend use of PEEP during OLV in clinically hypoxemic dogs with a closed thoracic cavity because it was not detrimental to cardiac function and DO_2 during OLV in clinically normal dogs with a closed thoracic cavity.

It has been established that PEEP can cause reductions in CO. Possible mechanisms include a reduction in venous return because of the increase in intrathoracic pressure,[1] increased right ventricular afterload,[22,23] leftward displacement of the interventricular septum,[24] depressed lung stretch reflex,[25,26] decreased left and right ventricular preload,[27] and altered ventricular function.[28,29] The exact mechanism for this effect is controversial and adverse hemodynamic effects generally are evident.[19,25,27,29-33] The negative effect of PEEP on hemodynamic variables has been documented in dogs with a closed thoracic cavity.[24,28,34] In animals with an intact rib cage, PEEP increases intrathoracic pressure and has a negative effect on cardiac function, however, the situation during OLV is not the same as that during TLV. During OLV, PEEP will be applied only to the ventilated lung whereas the nonventilated lung will become atelectatic. Absorption atelectasis of the nonventilated lung should allow expansion of the ventilated lung and limit increase in intrathoracic pressure. Therefore, the use of OLV in an animal with a closed thoracic cavity probably provided sufficient space for the ventilated lung to expand with PEEP, which prevented most of the negative effects of PEEP on hemodynamic variables.

Application of PEEP did not affect CO in the study because it did not have an effect on PVR. Pulmonary vascular resistance is a function of CO, MPAP, and PAWP.[22] In the study reported here, MPAP and PWAP were significantly increased but CO was unchanged, leading to a net effect of no change in the calculated PVR (Ohm's law). The volume of the lung and alveoli influences PVR because it alters the transmural pressure at the level of the capillaries.[35] Pulmonary vascular resistance is increased when lung volume is increased or decreased from FRC.[23,34-36] Positive end-expiratory pressure can affect PVR because of modification of FRC.[12,37] Thus, when the alveoli are collapsed,

PVR increases as a result of collapse of the alveolar capillaries. When the alveoli are subsequently reexpanded by use of PEEP, the expanded alveoli exert traction on the capillary wall to open the capillaries, thereby decreasing PVR. However, when the alveoli are overexpanded by use of excessive amounts of PEEP, transmural pressure increases and collapses the capillaries, which results in an increase in pulmonary arterial pressure. In this study, PVR was not affected by the amount of PEEP used, probably because collapsed alveoli were reexpanded without an induction of overdistension. Therefore, $PEEP_5$ did not affect PVR, and we believe $PEEP_5$ can be safely used during OLV with a closed thoracic cavity.

Pulmonary vascular resistance is also affected by transmural pressure,[35] recruitment of capillaries with increases in CO,[38,39] and HPV.[40,41] It was beyond the scope of our study to evaluate the effect of PEEP on PVR. However, it has been reported[42] that application of PEEP at < 5 cm H_2O is unlikely to increase PVR.

An increase in PVR in the ventilated lung as a result of PEEP applied during OLV can increase the amount of pulmonary shunting by redistributing blood flow from the ventilated areas to the nonventilated lung.[1] Values of PEEP in excess of 5 cm H_2O can increase PVR in the ventilated lung.[42] During OLV, the nonventilated lung represents a great potential for redistribution of blood flow after application of PEEP. However, during OLV, the nonventilated lung is subjected to HPV that reduces the amount of shunting by 30% to 40%.[1] Dogs have intense HPV[43] which should protect them against redistribution of blood flow during PEEP and OLV. However, anesthesia achieved by use of isoflurane or sevoflurane abolishes this phenomenon in a dose-dependent manner.[19,44] Because the dogs in our study were anesthetized with isoflurane, there could have been redistribution of blood flow to the nonventilated lung. We can assume the HPV response

did not change during the study because anesthesia was maintained at a constant depth. Because Q_S/Q_T and P_A-aO_2 improved and PVR did not change in this study, we can assume that the pulmonary blood flow was not redistributed to the nonventilated lung and that PEEP did not overstretch the recruited alveoli.

Shunt fraction improved with PEEP, indicating improvement in V/Q matching. However, this effect was not sufficient to induce a significant reduction of P_A-aO_2 and a significant augmentation of PaO_2. Application of PEEP increased the distention of poorly ventilated alveoli and recruited collapsed alveoli. Reduction of shunting did not increase PaO_2 significantly with $PEEP_5$; however, it did not induce a significant increase in the SaO_2 because of the sigmoid shape of the oxyhemoglobin dissociation curve. The values of PaO_2 observed in this study corresponded to the upper plateau of the oxygen-dissociation curve such that the nonsignificant increase in PaO_2 did not significantly increase SaO_2. Consequently, augmentation of the calculated CaO_2 was extremely limited because PaO_2 is only a negligible component in the equation to calculate CaO_2. In a study[37] in humans, the application of PEEP improved PaO_2 only in patients with a low PaO_2 (< 80 mm Hg) but not in patients with an initial PaO_2 > 80 mm Hg.[37] The proposed reason for this effect is that hypoxemic patients are more likely to have lung volumes below the FRC with increased PVR. With the use of PEEP, lung volume approaches FRC, which results in a decrease in PVR and an increase of blood flow to the dependent, ventilated lung.[11,37] The effect of PEEP would be more important in patients with pulmonary disease and low SaO_2. The negligible effect of PEEP on SaO_2 in our study limited any potential benefits of PEEP on DO_2.

The study reported here had several limitations. The small number of dogs entered in the study gave a limited power to our statistical analysis for the effect of PEEP

on CO and DO_2. However, O_{2ER}, which is another variable used to evaluate DO_2, had excellent power. Therefore, the fact that O_{2ER} was not significantly affected in this study would confirm that DO_2 was not significantly affected by the application of PEEP during OLV. Second, dogs evaluated were healthy dogs that did not have cardiopulmonary disease. Consequently, the detrimental effects of OLV on SaO_2 were minimal, which limited the opportunity for PEEP to exert a beneficial effect on DO_2.

A third limitation of the study was that the treatment groups were not randomized. Each dog served as its own control animal. As recommended in another report,[45] dogs were maintained on OLV for 15 minutes before recording data and then applying $PEEP_{2.5}$. The sequential application of $PEEP_{2.5}$ followed by $PEEP_5$ was used to mimic the clinical situation in which stepwise increases in PEEP are typically applied. It is possible that the beneficial effects of $PEEP_5$ were in part attributable to the preceding application of $PEEP_{2.5}$. Nevertheless, investigators in other studies[6,24,46,47] of cardiopulmonary effects of PEEP have generally recorded data after incremental increases in PEEP. It has also been recommended that PEEP be applied in an incremental fashion while concurrently measuring DO_2 to enable clinicians and researchers to optimize the effects of PEEP.[48]

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Table 5.1 Mean ± SE values for respiratory variables of 7 clinically normal anesthetized dogs with a closed thoracic cavity during OLV with 0 PEEP, $PEEP_{2.5}$, and $PEEP_5$.

Variable*	0 PEEP	$PEEP_{2.5}$	$PEEP_5$	*P*-value**	Power
PaO_2 (mm Hg)	170 ± 25	207 ± 26	245 ± 37	0.096	0.110
$PaCO_2$(mm Hg)	44 ± 2	42 ± 2	43 ± 3	0.402	0.427
PvO_2 (mm Hg)	60 ± 3	61 ± 3	62 ± 4	0.444	0.469
pHa	7.30 ± 0.02	7.30 ± 0.02	7.30 ± 0.03	0.869	0.878
HCO_3^-a (mEq/L)	22.0 ± 0.4	21.0 ± 0.4	22.0 ± 0.5	0.069	0.080
ABEa (mEq/L)	–4.1 ± 0.6	–4.9 ± 0.5	–4.7 ± 0.6	0.110	0.125
$P_{ET}CO_2$ (mm Hg)	35 ± 2	35 ± 2	36 ± 2	0.656	0.676
SaO_2 (%)	98.6 ± 0.2[a]	99.0 ± 0.2	99.2 ± 0.2[b]	0.022	NA
SvO_2 (%)	86.4 ± 1.3	86.8 ± 1.5	86.9 ± 1.5	0.739	0.754

* See list of abbreviations. ** Analysis of general effect; significance was defined as values of $P < 0.05$. NA = Not applicable. [a,b] Within a row, values with different superscript letter differ significantly ($P < 0.05$).

Table 5.2 Mean ± SE values for hemodynamic variables of 7 clinically normal anesthetized dogs with a closed thoracic cavity during OLV with 0 PEEP, $PEEP_{2.5}$, and $PEEP_5$.

Variable*	0 PEEP	$PEEP_{2.5}$	$PEEP_5$	*P*-value**	Power
SAP (mm Hg)	108 ± 6	109 ± 6	111 ± 6	0.826	0.838
DAP (mm Hg)	57 ± 3	60 ± 3	61 ± 2	0.452	0.477
MAP (mm Hg)	74 ± 3	76 ± 4	77 ± 3	0.516	0.540
RAP (mm Hg)	5.0 ± 0.3^a	7.0 ± 0.7^b	7.0 ± 0.3^b	0.007	NA
PAWP (mm Hg)	6 ± 1^a	8 ± 1^b	9 ± 1^b	< 0.001	NA
SPAP (mm Hg)	21 ± 1^a	24 ± 1^b	23 ± 1^b	0.033	NA
DPAP (mm Hg)	11 ± 1^a	12 ± 1	13 ± 1^b	0.049	NA
MPAP (mm Hg)	16 ± 1^a	17 ± 1^b	18 ± 1^b	0.011	NA
HR (beats/min)	117 ± 4	117 ± 5	115 ± 6	0.327	0.352
Core body temperature (°C)	36.5 ± 0.3	36.5 ± 0.3	36.7 ± 0.3	0.280	0.470

* See list of abbreviations. ** Analysis of general effect; significance was defined as values of $P < 0.05$. NA = Not applicable. ^{a,b} Within a row, values with different superscript letter differ significantly ($P < 0.05$).

Table 5.3 Mean ± SE values for calculated cardiopulmonary variables of 7 clinically normal anesthetized dogs with a closed thoracic cavity during OLV with 0 PEEP, $PEEP_{2.5}$, and $PEEP_5$.

Variable*	0 PEEP	$PEEP_{2.5}$	$PEEP_5$	*P*-value**	Power
CaO_2 (mL/dL)	21.6 ± 0.8	21.8 ± 0.9	22.0 ± 0.9	0.058	0.067
Qs/Q_T (%)	30 ± 2[a]	28 ± 1[b]	25 ± 1[b]	0.015	NA
DO_2 (mL/kg/min)	1,028 ± 136	1,105 ± 111	996 ± 144	0.472	0.496
PVRI (mm Hg/L/min/m^2)	2.0 ± 0.2	2.0 ± 0.2	2.0 ± 0.3	0.141	0.158
SVRI (mm Hg/L/min/m^2)	15 ± 2	13 ± 1	15 ± 1	0.157	0.176
O_{2ER} (%)	12.4 ± 0.1	12.3 ± 0.1	12.5 ± 0.2	0.966	0.968
CI (L/min/m^2)	5.1 ± 0.6	5.4 ± 0.5	4.8 ± 0.6	0.416	0.441
V_D/V_T (%)	21 ± 2	18 ± 2	18 ± 1	0.227	0.249
P_A-aO_2 (mm Hg)	375 ± 27	340 ± 27	301 ± 37	0.089	0.102
PAO_2 (mm Hg)	545 ± 6	547 ± 6	546 ± 7	0.402	0.427

* See list of abbreviations. ** Analysis of general effect; significance was defined as values of $P < 0.05$. NA = Not applicable. [a,b] Within a row, values with different superscript letter differ significantly ($P < 0.05$).

CHAPTER VI

CARDIOPULMONARY EFFECTS OF ONE-LUNG VENTILATION IN ANESTHETIZED DOGS WITH CLOSED AND OPEN THORACIC CAVITY

A. INTRODUCTION AND HYPOTHESIS

It has been shown that PaO_2 may be decreased and Q_S/Q_T increased during chest surgery.[1-3] Isolation and selective ventilation of one lung, OLV,[4] has been absolutely indicated for many thoracic procedures such as an infected or purulent lung or any tracheobronchial tree disruption to protect and allow adequate ventilation of the normal lung.[4-6] It is also the default technique to use in thoracoscopy procedures in humans[7,8] and it has been used in animals as well.[9-12] Conversion from TLV to OLV significantly decreases PaO_2, and SaO_2, and increases Q_S/Q_T.[13-15]

Generally, OLV is used for many open chest procedures.[13,14,16,17] The initiation of OLV during closed chest, although less common, has also been used in both clinical[6,18] and experimental situations.[19-21]

The independent effects of thoracotomy and OLV on hemodynamic parameters during closed or open chest procedures have been described.[17,19,22,23] Similarly, the respiratory consequences have been studied.[2,3,13,14,17,19,22,23] One-lung ventilation induces different cardiopulmonary effects depending on whether the chest is closed or open. Open chest eliminates negative intrapleural pressure, which induces more atelectasis than

closed chest. Therefore the effect of OLV on DO_2 should be different for closed and open chest.

The purpose of the present study is to evaluate if there is an interaction or association between TLV-OLV and closed-open chest in determining cardiopulmonary parameters, particularly DO_2. Oxygen delivery integrates the respiratory, cardiovascular, and microvascular systems. It is a function of CO and CaO_2.[24]

We hypothesized that the effect of OLV on DO_2 is different in closed and open chest in anesthetized dogs in right lateral recumbency.

B. MATERIALS AND METHODS

Animals

Seven healthy dogs, according to physical and hematological exams, weighing between 25 and 30 kg, with ages between 2 and 5 years old, and mixed gender, were included in this study. Food was withdrawn 12 hours before the study. This study was approved by Colorado State University Animal Care and Use Committee. Dogs were adopted at the end of the study.

Procedure

Each dog was its own control. The dogs received no medications prior to induction of anesthesia. An 18-gauge over-the-needle catheter[a] was inserted in a cephalic vein and a bolus of lactated Ringer's solution[b] (10 mL/kg) was administered IV. Induction of anesthesia was accomplished by IV administration of propofol[c] (3 to 4 mg/kg) and diazepam[d] (0.3 mg/kg). Endotracheal intubation was performed, and anesthesia was maintained with an end-tidal concentration of isoflurane[e] of 1.85% to

1.95% (approx 1.5 times the minimum alveolar concentration) in oxygen, delivered through a precision out-of-circuit vaporizer[f] in a semiclosed circle rebreathing system. An agent analyzer[g] was used to measure end-tidal isoflurane concentration. An esophageal temperature probe[h] was advanced to the region of the heart base to measure core body temperature. Maintenance fluids consisted of IV administration of lactated Ringer's solution[b] (5 mL/kg/h) and a solution of dextrans[i] (5 mL/kg/h). To facilitate intermittent positive-pressure ventilation, the dogs were administered a paralytic agent (atracurium[j]; 0.2 mg/kg, IV as a bolus, followed by 0.1 mg/kg IV, repeated as needed). A nerve stimulator[k] placed over the peroneal nerve was used to assess muscle relaxation by enabling investigators to observe the response to a train-of-four electrical stimulation.

The dogs were positioned in right lateral recumbency. A volume-limited ventilator[l] was adjusted to provide a baseline $PaCO_2$ of 35 to 45 mm Hg. End-tidal partial pressure of carbon dioxide was monitored by use of a side-stream capnograph[m] connected to the endotracheal tube. Once a $PaCO_2$ of 35 to 45 mm Hg was achieved and maintained, respiratory rate (7 to 16 breaths/min) and VT (14 to 15 mL/kg) were not changed during the remainder of the study. A respirometer[n] was used to measure expiratory VT.

Hemodynamic and cardiorespiratory variables

A 20-gauge over-the-needle catheter[a] was inserted in the dorsal pedal artery. Systolic arterial pressure, DAP, and MAP were recorded continuously on a pressure monitor.[o] Results of ECG and pulse oximetry[p] were also recorded on the monitor. A 7.5-F Swan-Ganz catheter[q] was inserted in the pulmonary artery through an 8-F introducer[r] that had been inserted in the jugular vein; characteristic waveforms were used to guide

proper placement of the catheter in the pulmonary artery. Each catheter was connected to fluid-filled pressure transducers[s] and zeroed at the level of the right atrium.

Systolic pulmonary artery pressure, DPAP, and MPAP were also recorded continuously on a pressure monitor.[t] Pulmonary artery wedge pressure, RAP and HR were recorded. Cardiac output was measured by use of the thermodilution technique. Ten milliliters of ice-cold saline (0.9% NaCl) solution was injected into the right atrium, and the mean of 3 measurements was determined by the use of a CO computer.[u]

Blood gas analysis[v] was performed on heparinized blood samples. Arterial and mixed venous blood samples were collected via the catheters inserted in the pedal and pulmonary arteries respectively, and samples were analyzed immediately after collection to determine PaO_2, PvO_2, SaO_2, SvO_2, $PaCO_2$, pHa, HCO_3^-a, and ABEa.
Values were calculated for the following variables: $Cc'O_2$, P_AO_2, Q_S/Q_T, CaO_2, CvO_2, $P_A\text{-}aO_2$, DO_2, CI, O_{2ER}, PVRI, SVRI, and V_D/V_T. (See appendix for formulas).

Collection of data

Data was collected during TLV after the baseline reading of $PaCO_2$ was stable within the value specified above. The left bronchus of the dog was then obstructed using a bronchial blocker[w] inserted through a multiple-port airway adapter[x] under bronchoscopy[y]. Once the left bronchus was blocked, 15 minutes were allowed for equilibration, and then data corresponding to closed-chest OLV was collected.

After the collection of the data for closed chest was completed, the bronchial blocker was deflated and TLV resumed. The left side of the thorax that had been previously clipped was prepared for surgery. The thoracic cavity was opened as for a left-sided thoracoscopic approach inserting 12 mm cannulas[z] at the fourth, sixth and tenth

intercostal spaces. Again, 15 minutes were allowed for equilibration before the data for open chest TLV was collected. Finally, the left bronchus was blocked and after the equilibration period data for open chest OLV was recorded.

At the completion of the experiment, analgesia was maintained with an IV fentanyl[aa] infusion and a transdermal fentanyl patch[bb]. Dogs were recovered in a critical care unit under standard care as for client owned animals.

Statistical analysis

An ANOVA for repeated measurements[25] was used to statistically evaluate the effects of the interaction between TLV-OLV and closed-open chest on the cardio-respiratory parameters. A value of $P < 0.05$ was set as a level of significance. Data is presented as mean ± SE.

C. RESULTS

Results for respiratory, hemodynamic and calculated cardiopulmonary parameters for the effect of the interaction between TLV-OLV and closed-open chest are shown in tables 6.1, 6.2 and 6.3 respectively. Figures 6.1 thru 6.4 show the parameters that were significantly affected by the interaction.

There was a significant effect of the interaction on Q_S/Q_T ($P = 0.034$), PaO_2 ($P = 0.006$), CaO_2 ($P = 0.005$) and $P_{A\text{-}a}O_2$ ($P = 0.008$), but not on SaO_2 ($P = 0.211$). Other cardiopulmonary variables were not affected by the interaction. As a net result of the interaction between TLV-OLV and closed-open chest on hemodynamic and respiratory variables DO_2 was not significantly altered ($P = 0.798$).

D. DISCUSSION

Cardiac index was not affected by the interaction between TLV-OLV and closed-open chest, and the significant variation in CaO_2 alone did not result in any change in DO_2. In other studies, neither opening of the thoracic cavity nor the individual effect of OLV during closed or open chest procedures produced any variation in CI.[17,19,22,23] Respiratory parameters such as PaO_2 and SaO_2, on the other hand, have been consistently reported as showing significant decreases with chest opened during TLV,[2,3,17,23] chest opened during OLV,[13,14,17,22] and chest closed during OLV,[19] as a result of increase in Q_S/Q_T, which also has been shown to consistently increase due to the individual effects of open chest and OLV.[14,16,17,23]

In the present study, it was shown that variations in Q_S/Q_T, which in turn resulted in significant effects on PaO_2, CaO_2 and $P_{A\text{-}a}O_2$, are the result of a significant interaction between TLV-OLV and closed-open chest. Thus, the extent of the variations in Q_S/Q_T, PaO_2, CaO_2, and $P_{A\text{-}a}O_2$ as the result of switching from TLV to OLV depends upon the chest being closed or open.

Arterial oxygen content is a function of PaO_2, SaO_2 and Hb concentration.[24] In this study, although the interaction affected Q_S/Q_T with an extended significant effect on PaO_2, SaO_2 was not affected by the interaction. The changes in PaO_2, however, were enough to cause a statistically significant effect on CaO_2, but this change was not biologically significant. The reason for this seeming discrepancy may be that throughout the experiment PaO_2 was kept well above 70 mm Hg, which is the point where the oxygen dissociation curve flattens. Thus, SaO_2 stayed very high on the top-flat portion of the dissociation curve where any variation on PaO_2 does not lead to significant changes in

SaO_2.[26] A more marked response in SaO_2 may be induced in patients with compromised lung function.

The explanation for the interactive effect between TLV-OLV and closed-open chest may be better understood starting with the individual effects of each factor.

During the lateral position on no anesthetized patients, there is a good V/Q matching because most of the blood flow and ventilation go to the dependent lung. Thus, Qs/Qt is not affected significantly.[27]

In anesthetized patients, the reduction of FRC is more pronounced on the dependent lung as a result of loss of lung volume with anesthesia, shifted mediastinum impeding expansion of the dependent lung, and pressure from abdominal contents.[4,27-29] In our study, there was a relatively small Qs/Qt of 8% during closed chest TLV, most likely due to the effect of anesthesia and paralysis. General anesthesia does not greatly change the perfusion distribution, but has an important effect on ventilation with the nondependent lung receiving ventilation in excess of perfusion,[30,31] and the dependent lung receiving more perfusion than the nondependent lung, which results in V/Q mismatch and increased Qs/Qt.[27]

Opening the thoracic cavity produces atelectasis and reduction of the FRC, increase in Qs/Qt, and impairing of the V/Q distribution, which results in a decreased PaO_2.[1,27,32,33]

In the lateral position, opening of the nondependent side of the thorax during TLV increases compliance and FRC of the nondependent lung, and decreases FRC in the dependent lung.[4] In our study, we used thoracoscopy cannulas to create the open chest situation keeping the thoracic wall intact, which probably determined that during this open chest situation, since the nondependent lung was restricted by the thoracic wall, it

was not able to expand as much as it would in a complete thoracotomy, neither to increase its FRC and compliance. Shunt fraction increased in our study during TLV when the thorax was opened, accompanied by the corresponding decreased PaO_2 and CaO_2 and increased $P_{A\text{-}a}O_2$.

Shunt fraction was different for TLV depending on whether the chest was closed or open, with a higher Q_S/Q_T occurring during open chest. For closed chest OLV, Q_S/Q_T was higher than for TLV with either closed or open chest. However, opposite to what may be expected, there was not a further increase in Q_S/Q_T during open chest OLV respect to closed chest OLV, instead, its value of about 30% was quite similar to that during closed chest OLV. Other studies during OLV have shown similar values of Q_S/Q_T.[14,16,19,22,34]

With OLV, absorption atelectasis of the nonventilated lung occurs after occlusion of its main bronchus,[35] and the V_T that was being delivered to two lungs is delivered to a single lung, increasing its V/Q.[27] Thus, when OLV is started, the nondependent lung that had most of the ventilation, poorer perfusion and a high V/Q during TLV, is now collapsed. The ventilation is then redistributed to the dependent lung that had favored perfusion but poorer ventilation during TLV. As a result, the decreased FRC of the dependent lung during TLV may be improved during OLV with this redistribution of ventilation going to the better perfused dependent lung, which probably helps some of its low V/Q areas to approach a V/Q matching closer to optimal.

While the nondependent lung is not receiving ventilation during OLV, blood flow through this lung becomes an obligatory right-to-left shunt.[27,36] Hypoxic pulmonary vasoconstriction,[35,37-40] a mechanism to divert blood flow away from underventilated areas to better ventilated areas of the lung, takes place to decrease the amount of shunt

originated by OLV.[27] The distribution of the perfusion is thus an important part in determining the amount of shunt during OLV.[27]

Given that Qs/Qt during TLV anesthesia with closed and open chest is caused mainly by maldistribution of the ventilation, the effect of the interaction between TLV-OLV and closed-open chest on the behavior of Qs/Qt, PaO_2, CaO_2, and $PA\text{-}aO_2$ may be summarized in part as the result of a combination of effects. These include a counteracting-like effect that OLV has on the ventilation distribution in the lateral position, and a prevailing effect of the perfusion distribution with OLV (i.e.: remaining blood flow to the nonventilated lung despite HPV) determining the amount of Qs/Qt.

Intrapleural pressure is less negative at the bottom than at the top areas of the lungs because of the weight of the lungs.[41] Intrapleural pressure then is more negative around the nondependent than around the dependent lung in the lateral position. The lack of a difference in the amount of Qs/Qt during OLV with closed and open chest may also be associated with the relatively smaller increase in the pressure that is necessary to reach atmospheric pressure around the dependent than around the nondependent lung, when the thorax is open. Thus, opening the thorax would induce a smaller change in pressure around the dependent than around the nondependent lung, resulting in more atelectatic shunt-increasing areas over the nondependent, ventilated lung than over the dependent, ventilated lung during OLV.

In conclusion, OLV induces a similar amount of Qs/Qt during closed and open chest as a result of the effect of the interaction between TLV-OLV and closed-open chest. Variations in PaO_2, $PA\text{-}aO_2$ and CaO_2 followed the behavior of Qs/Qt. While circulatory parameters are not affected, oxygenation also can be expected to be the same during OLV with either closed or open chest. As a net result DO_2 is not affected. However, it is

interesting that despite CaO_2 being similar for closed and open chest, both CI and DO_2, increased by 20% during OLV with open chest with respect to OLV with closed chest. This is an important consideration given that OLV is used mostly with open chest.

A limitation of the present study is that it was performed on healthy dogs. In patients with compromised cardiopulmonary function, Q_S/Q_T may be further affected and the respiratory effects of the interaction may be more pronounced, probably extending its effect to SaO_2 and DO_2. Another limitation is that the treatments were not applied randomly, which may have affected the results of this experiment.

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Fig. 6.1 Shunt fraction of 7 clinically normal anesthetized dogs for the interaction between TLV-OLV and closed-open chest ($P = 0.034$).

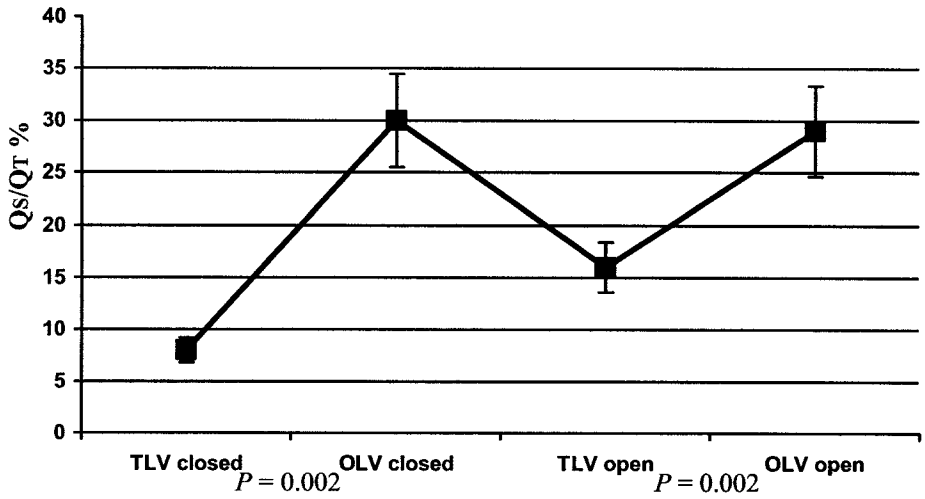

Fig. 6.2 Arterial oxygen partial pressure of 7 clinically normal anesthetized dogs for the interaction between TLV-OLV and closed-open chest ($P = 0.006$).

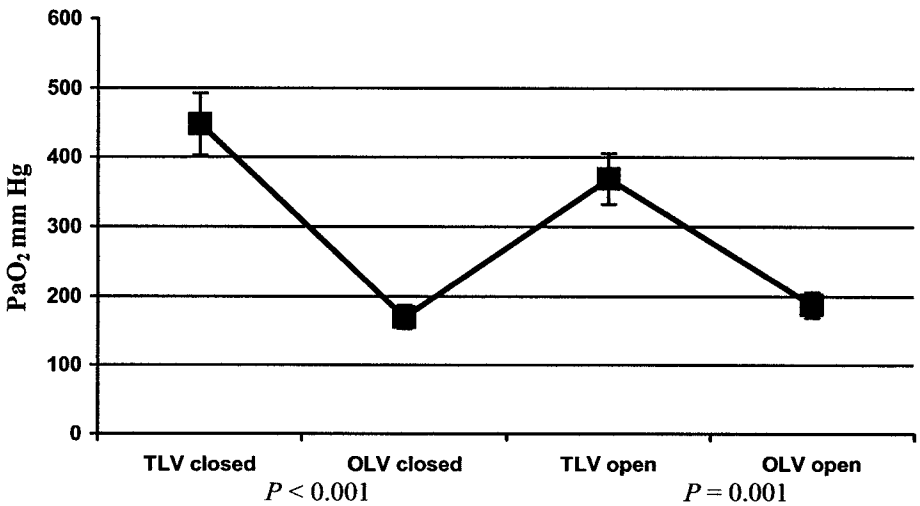

Fig. 6.3 Arterial oxygen content of 7 clinically normal anesthetized dogs for the interaction between TLV-OLV and closed-open chest ($P = 0.005$).

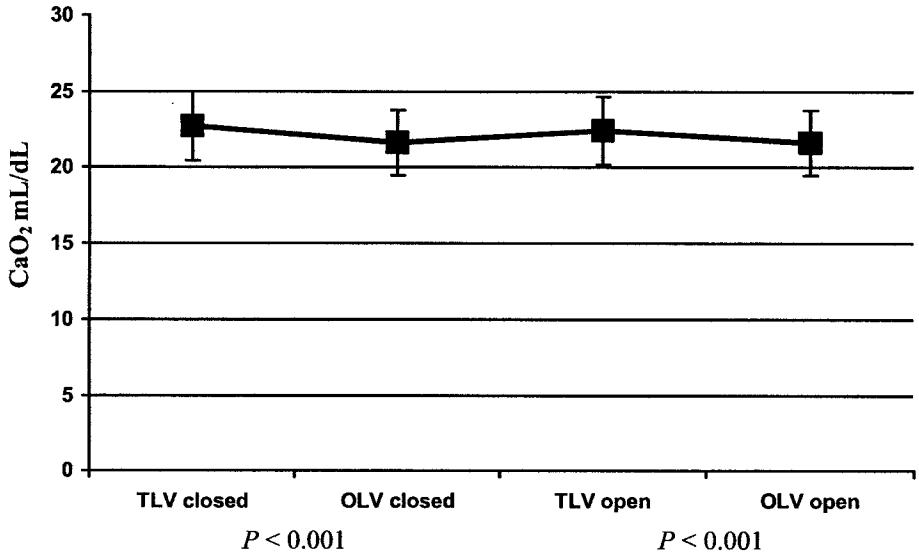

Fig. 6.4 Alveolar-arterial oxygen partial pressure difference of 7 clinically normal anesthetized dogs for the interaction between TLV-OLV and closed-open chest ($P = 0.008$).

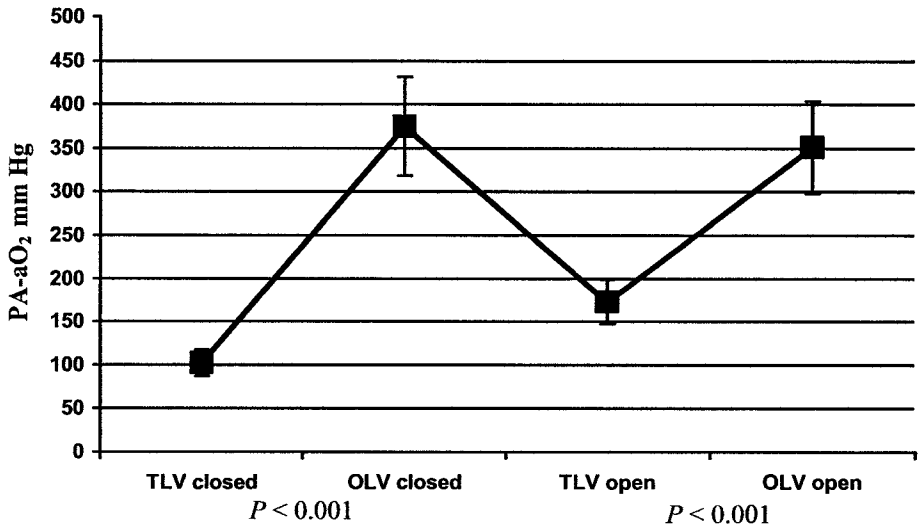

Table 6.1 Mean ± SE values for respiratory variables of 7 clinically normal anesthetized dogs for the interaction between TLV-OLV and closed-open chest.

Variable*	TLV CLOSED	OLV CLOSED	TLV OPEN	OLV OPEN	*P*-value
PaO_2 (mm Hg)	448 ± 24	170 ± 25	369 ± 39	188 ± 36	0.006**
$PaCO_2$ (mm Hg)	40 ± 1	44 ± 2	41 ± 1	44 ± 1	0.522
PvO_2 (mm Hg)	68 ± 3	60 ± 3	67 ± 5	58 ± 3	0.906
pHa	7.35 ± 0.01	7.30 ± 0.02	7.33 ± 0.01	7.30 ± 0.01	0.773
HCO_3^-a (mEq/L)	22.0 ± 0.5	22.0 ± 0.4	22.0 ± 0.3	22.0 ± 0.4	0.409
ABEa (mEq/L)	-4.0 ± 0.5	-4.1 ± 0.6	-4.5 ± 0.3	-4.9 ± 0.5	0.542
$P_{ET}CO_2$ (mm Hg)	35 ± 1	35 ± 2	34 ± 1	35 ± 1	0.993
SaO_2 (%)	99.90 ± 0.02	98.60 ± 0.24	99.70 ± 0.13	98.70 ± 0.30	0.211
SvO_2 (%)	87.3 ± 3.7	86.4 ± 1.3	89.1 ± 1.6	84.6 ± 1.6	0.352
* See list of abbreviations ** *P*-value shows an interaction at $P < 0.05$ for TLV-OLV and closed-open chest.					

Table 6.2 Mean ± SE values for hemodynamic variables of 7 clinically normal anesthetized dogs for the interaction between TLV-OLV and closed-open chest.

Variable*	TLV CLOSED	OLV CLOSED	TLV OPEN	OLV OPEN	*P*-value
SAP (mm Hg)	95 ± 5	108 ± 6	109 ± 5	113 ± 10	0.397
DAP (mm Hg)	50 ± 2	57 ± 3	61 ± 3	64 ± 6	0.577
MAP (mm Hg)	64 ± 3	74 ± 3	78 ± 3	80 ± 7	0.343
RAP (mm Hg)	5.0 ± 0.3	5.0 ± 0.3	8.0 ± 0.8	9.0 ± 0.7	0.156
PAWP (mm Hg)	6 ± 1	6 ± 1	8 ± 0.7	10 ± 1	0.153
SPAP (mm Hg)	19 ± 1	21 ± 1	25 ± 1	28 ± 2	0.253
DPAP (mm Hg)	9 ± 1	11 ± 1	15 ± 1	15 ± 1	0.412
MPAP (mm Hg)	14 ± 1	16 ± 1	18 ± 1	22 ± 2	0.172
HR (beats/min)	107 ± 5	117 ± 4	117 ± 6	119 ± 6	0.161
CORE BODY Temperature (C°)	36.5 ± 0.3	36.5 ± 0.3	36.8 ± 0.3	36.9 ± 0.3	0.355
* See list of abbreviations					

Table 6.3 Mean ± SE values for calculated cardiopulmonary variables of 7 clinically normal anesthetized dogs for the interaction between TLV-OLV and closed-open chest.

Variable*	TLV CLOSED	OLV CLOSED	TLV OPEN	OLV OPEN	*P*-value
CaO_2 (mL/dL)	22.7 ± 0.8	21.6 ± 0.8	22.4 ± 0.8	21.6 ± 0.8	0.005**
Q_S/Q_T (%)	8 ± 1	30 ± 2	16 ± 1	29 ± 2	0.034**
DO_2 (mL/kg/min)	876 ± 78	1,028 ± 136	1,108 ± 114	1,227 ± 183	0.798
PVRI (mm Hg/L/min/m^2)	2.0 ± 0.3	2.0 ± 0.2	2.0 ± 0.3	2.0 ± 0.2	0.734
SVRI (mm Hg/L/min/m^2)	15 ± 1	15 ± 2	14 ± 1	13 ± 2	0.577
O_{2ER} (%)	12.6 ± 0.4	12.4 ± 0.1	10.7 ± 0.2	14.2 ± 0.2	0.334
CI (L/min/m^2)	4.2 ± 0.4	5.1 ± 0.6	5.3 ± 0.5	6.1 ± 0.9	0.886
V_D/V_T (%)	12 ± 3	21 ± 2	17 ± 1	22 ± 2	0.164
$P_{A-a}O_2$ (mm Hg)	102 ± 20	375 ± 27	173 ± 38	351 ± 35	0.008**
P_AO_2 (mm Hg)	551 ± 6	545 ± 6	543 ± 2	545 ± 5	0.522
* See list of abbreviations ** *P*-value shows interactions at $P < 0.05$ for TLV-OLV and closed-open chest.					

CHAPTER VII

CARDIOPULMONARY EFFECTS OF POSITIVE END-EXPIRATORY PRESSURE DURING ONE-LUNG VENTILATION IN ANESTHETIZED DOGS WITH CLOSED AND OPEN THORACIC CAVITY

A. INTRODUCTION AND HYPOTHESIS

Selective ventilation of the lung, OLV,[1] is a common technique during thoracic surgery including minimally invasive procedures.[1-3] One-lung ventilation is also used with a closed chest.[4,5] One-lung ventilation increases Q_S/Q_T, and results in significant reductions in PaO_2 and SaO_2.[6-8] Increased Q_S/Q_T during OLV is not only related to the amount of blood flowing through the atelectatic lung despite HPV, but also is related to the amount of blood circulating through atelectatic areas in the ventilated lung.[1,9]

Positive end-expiratory pressure has been used as a rapid method to improve gas exchange by increasing the resting lung volume at the end of expiration. It increases FRC contributing to recruitment of alveoli, preventing airway closure and improving gas exchange.[10-12] However, the use of PEEP may result in a reduction of CO.[13-16] Decreased venous return,[1] reduced left and right ventricular preload,[13] increased right ventricular afterload,[13-15] leftward displacement of the interventricular septum,[16] and obstruction of the right atrial filling by the rise of intrapleural pressure[17] have been proposed as possible mechanisms for the decrease in CO with PEEP. Intrapleural pressure is an important

factor related to venous return[1] and appears to be an important part of the mechanisms involved in the decrease of CO with PEEP.[1,13,16,17] Intrathoracic pressure influences the pressure gradient necessary for blood to flow from the abdomen or venous return to the thorax, which determines the actual amount of blood available to fill the ventricle.[13] An increase in intrathoracic pressure affects ventricular distensibility or compliance as well[13] and may induce changes in the transmural pressure of the heart affecting afterload.[18]

Positive end-expiratory pressure and opening of thoracic cavity are both factors that affect intrathoracic pressure.[17,19] Intrapleural pressure is kept negative during closed chest by the interaction between the lungs and the chest wall, but in an open chest situation, the outward elastic recoil of the chest wall is lost and intrathoracic pressure equals atmospheric pressure.[20] The negative effect of PEEP on hemodynamic variables has been demonstrated with a closed chest.[21-24] During thoracoscopic procedures the thoracic cavity is exposed to atmospheric pressure, but since only cannulas are inserted in a few intercostals spaces, the shape and volume of the chest wall restraining the lungs is kept intact as in a closed chest situation.[25] However, the use of OLV during thoracoscopy may provide some space for the ventilated lung to expand since the nonventilated lung is collapsed, which probably will lessen the negative effect of PEEP. Therefore, the way that cardiorespiratory parameters respond to the use of PEEP may vary depending upon the chest being closed or open.

The objective of the present study is to determine if during OLV in dogs, there is a significant interaction between the use of PEEP applied to the dependent lung and the closed-open chest situation having an effect on cardiorespiratory parameters, with special attention to DO_2. We hypothesized that the application of PEEP during OLV does not

have the same effect on DO_2 in anesthetized dogs with closed and open chest in right lateral recumbency.

B. MATERIALS AND METHODS

Animals

Seven healthy dogs, as determined on the basis of results of physical examination, a CBC count, and serum biochemical analysis, were included in the study. Dogs were sexually intact, of both sexes, and weighed between 25 and 30 kg. Dogs were between 2 and 5 years old. Food was withheld from each dog beginning 12 hours before the onset of the study. The study was approved by the Colorado State University Animal Care and Use Committee. Dogs were adopted at the end of the study.

Procedure

Each dog was its own control. The dogs received no medications prior to induction of anesthesia. An 18-gauge over-the-needle catheter[a] was inserted in a cephalic vein and a bolus of lactated Ringer's solution[b] (10 mL/kg) was administered IV. Induction of anesthesia was accomplished by IV administration of propofol[c] (3 to 4 mg/kg) and diazepam[d] (0.3 mg/kg). Endotracheal intubation was performed, and anesthesia was maintained with an end-tidal concentration of isoflurane[e] of 1.85% to 1.95% (approx 1.5 times the minimum alveolar concentration) in oxygen, delivered through a precision out-of-circuit vaporizer[f] in a semiclosed circle rebreathing system. An agent analyzer[g] was used to measure end-tidal isoflurane concentration. An esophageal temperature probe[h] was advanced to the region of the heart base to measure core body temperature. Maintenance fluids consisted of IV administration of lactated Ringer's

solution[b] (5 mL/kg/h) and a solution of dextrans[i] (5 mL/kg/h). To facilitate intermittent positive-pressure ventilation, the dogs were administered a paralytic agent (atracurium[j]; 0.2 mg/kg, IV as a bolus, followed by 0.1 mg/kg IV, repeated as needed). A nerve stimulator[k] placed over the peroneal nerve was used to assess muscle relaxation by enabling investigators to observe the response to a train-of-four electrical stimulation.

The dogs were positioned in right lateral recumbency. A volume-limited ventilator[l] was adjusted to provide a baseline $PaCO_2$ of 35 to 45 mm Hg. End-tidal partial pressure of carbon dioxide was monitored by use of a side-stream capnograph[m] connected to the endotracheal tube. Once a $PaCO_2$ of 35 to 45 mm Hg was achieved and maintained, respiratory rate (7 to 16 breaths/min) and VT (14 to 15 mL/kg) were not changed during the remainder of the study. A respirometer[n] was used to measure expiratory VT.

Hemodynamic and cardiorespiratory variables

A 20-gauge over-the-needle catheter[a] was inserted in the dorsal pedal artery. Systolic arterial pressure, DAP, and MAP were recorded continuously on a pressure monitor.[o] Results of ECG and pulse oximetry[p] were also recorded on the monitor. A 7.5-F Swan-Ganz catheter[q] was inserted in the pulmonary artery through an 8-F introducer[r] that had been inserted in the jugular vein; characteristic waveforms were used to guide proper placement of the catheter in the pulmonary artery. Each catheter was connected to fluid-filled pressure transducers[s] and zeroed at the level of the right atrium.

Systolic pulmonary artery pressure, DPAP, and MPAP were also recorded continuously on a pressure monitor.[t] Pulmonary artery wedge pressure, RAP and HR were recorded. Cardiac output was measured by use of the thermodilution technique. Ten

milliliters of ice-cold saline (0.9% NaCl) solution was injected into the right atrium, and the mean of 3 measurements was determined by the use of a CO computer.[u]

Blood gas analysis[v] was performed on heparinized blood samples. Arterial and mixed venous blood samples were collected via the catheters inserted in the pedal and pulmonary arteries respectively, and samples were analyzed immediately after collection to determine PaO_2, PvO_2, SaO_2, SvO_2, $PaCO_2$, pHa, HCO_3^-a, and ABEa.
Values were calculated for the following variables: $Cc'O_2$, P_AO_2, Q_S/Q_T, CaO_2, CvO_2, $P_A\text{-}aO_2$, DO_2, CI, O_{2ER}, PVRI, SVRI, and V_D/V_T. (See appendix for formulas).

Collection of data

The left bronchus of the dog was obstructed using a bronchial blocker[w] inserted through a multiple-port airway adapter[x] under bronchoscopy[r]. Once the left bronchus was blocked, 15 minutes were allowed for equilibration, and then data corresponding to closed chest OLV was collected.

After the collection of the data for closed chest OLV was completed, $PEEP_{2.5}$ was applied and after the 15 minutes for equilibration, the data was collected for OLV-$PEEP_{2.5}$. Next, $PEEP_5$ was applied and data for OLV-$PEEP_5$ was collected after the equilibration period of 15 minutes. One-lung ventilation with 0 PEEP was resumed. The left side of the thorax that had been previously clipped was prepared for surgery. The thoracic cavity was opened as for a left-sided thoracoscopic approach inserting 12 mm cannulas[z] at the fourth, sixth and tenth intercostal spaces. Again, 15 minutes were allowed for equilibration before the data for open chest OLV was collected. Finally, as it was done for closed chest, PEEP was applied during open chest and the data for OLV-$PEEP_{2.5}$ and OLV-$PEEP_5$ with open chest was recorded.

At the completion of the experiment, analgesia was maintained with an IV fentanyl[aa] infusion and a transdermal fentanyl patch[bb]. Dogs were recovered in a critical care unit under standard care as for client owned animals.

Statistical analysis

An ANOVA for repeated measurements[26] was used to statistically evaluate the effects of the interaction between OLV-$PEEP_{2.5}$-$PEEP_5$ and closed-open chest on the cardiorespiratory parameters. The level of significance was set at $P < 0.05$. Data is presented as mean ± SE.

C. RESULTS

Results for respiratory, hemodynamic and calculated cardiopulmonary variables for the effect of the interaction between OLV-$PEEP_{2.5}$-$PEEP_5$ and closed-open chest are shown in tables 7.1, 7.2, and 7.3 respectively. Figures 7.1 and 7.2 show the parameters that were significantly affected by the interaction.

There was a significant effect of the interaction on PAWP ($P = 0.010$) and on MPAP ($P = 0.004$). There was no significant interaction between OLV-$PEEP_{2.5}$-$PEEP_5$ and closed-open chest affecting other hemodynamic and respiratory parameters. As a net result DO_2 was not significantly altered ($P = 0.496$).

D. DISCUSSION

The interaction between OLV-$PEEP_{2.5}$-$PEEP_5$ and closed-open chest did not have any effect on DO_2. This interaction was significant only for changes in MPAP and PAWP. There were no significant interactive effects on the rest of the cardiopulmonary

variables. Positive end-expiratory pressure has been related to increases in pulmonary artery pressure because it increases transmural pressure at the level of the capillaries, which in turn increases PVR.[12,27] However, PVR stayed constant throughout this study. Positive end-expiratory pressure of less than 5 cm H_2O has been shown to be unlikely to increase PVR,[28] therefore, the changes observed in MPAP and PAWP were probably related to a different factor, and not to an increase in PVR. In this study, the increases in MPAP and PAWP were more likely associated with the variations in intrathoracic pressure determined by the interaction between PEEP and the closed-open chest situation.

Positive end-expiratory pressure increases intrapleural pressure but in an amount much less than the PEEP that has been applied.[17] More than half of the pressure resulting from the use of PEEP is absorbed by the pulmonary transmural pressure, which increases along with PEEP.

In our study we used normal dogs. In a normal lung, there is an intrapleural pressure of approximately –5 cm H_2O at the end of the expiration.[19] As an example, if a proportion of less that half of the PEEP, such as 40%, is transmitted to the intrapleural pressure, then the use of $PEEP_{2.5}$ would result in an increase of 1 cm H_2O, and the use of $PEEP_5$ would result in an increase of 2 cm H_2O in the intrapleural pressure in a closed chest. Accordingly the trend of the increase in MPAP and PAWP during closed chest was proportional to the increasing level of PEEP used in this study.

The use of positive end-expiratory pressure has its negative effect on CO mostly when the thoracic cavity is closed.[29,30] Also with a closed chest, since the lung cannot overinflate as much as it would with intercostal thoracotomy, the use of PEEP induces an augmentation of PVR.[31] In the present study, the thoracic cavity was opened by thoracoscopy. Thoracoscopy is considered as an open chest situation because the negative

intrapleural pressure is abolished by placement of open cannulas; however, the rib cage is still present as for a closed chest. Overinflation of the lungs is then limited. Therefore, the effect of PEEP on hemodynamic variables during thoracoscopy should be similar to the effect during a closed chest situation. The use of OLV, however, might provide enough space in the thoracic cavity for the ventilated lung to expand as during an open chest situation. Positive end-expiratory pressure may then not interfere with venous return, PVR and CO. The use of thoracoscopy can be considered then as a hybrid situation in which the effect of the application of PEEP may be difficult to predict.

In this study, the use of increasing levels of PEEP during open chest had a different effect on MPAP and PAWP with respect to closed chest. These pressures stayed equally higher than during closed chest at any point, and during open chest the difference of pressure values among the various data points was not as marked as it was for closed chest. It seems that the trend of these pressures to rise proportionally along with the use of increasing levels of PEEP was abolished by opening the chest. This is probably because atmospheric pressure with an open chest keeps constant around intrathoracic structures independently of the level of PEEP used, and OLV provided enough room for the ventilated lung to expand.

The use of higher levels of PEEP in our study might have affected CO and produced a different response for closed or open chest. However, despite the role of intrapleural pressure in relation to venous return[1] and the decreased CO with PEEP,[1,13,16,17] a considerable proportion of the negative effect of PEEP occurs independently of the closed-open chest situation.[32-37] This is related to increased pericardial and right atrial pressure from mechanical interaction between the heart and the lungs exerting traction as a result of PEEP.[32,33,36,38] There is a relationship between

pericardial pressure and RAP, with both increasing linearly with PEEP.[39] This increase in pericardial pressure has been shown to happen both with closed and open chest. [32-38]

The decrease in CO with PEEP is greater when the distension of the lung is adjacent to the right heart. An increase in RAP is more related to a decreased stroke volume than to an increase in left atrial pressure.[32] The negative effects of PEEP during OLV decreasing CO are less pronounced than during TLV.[32,40] There is also a difference in the degree of reduction in CO depending on the lung that is receiving PEEP, with a greater increase in pericardial pressure and decrease in CO with PEEP on the right lung than with PEEP applied to the left lung.[40]

The small amount of PEEP used in this study was likely safe enough to produce no negative effects on CO. The use of higher levels of PEEP or dogs with diseased lungs may have resulted in a more profound effect over CO or DO_2.

The use of healthy dogs was a limitation in this study because healthy individuals are less likely to be affected by the negative effects of PEEP. It would be interesting to repeat this study with the use of clinical patients with impaired gas exchange. Another limitation of the study was that the treatment groups were not randomized. The sequential application of PEEP in 2.5 cm H_2O increments was performed to mimic the clinical situation where stepwise increases in PEEP are usually applied. Other studies of the cardiopulmonary effects of PEEP generally recorded data after incremental increases in PEEP.[7,16,27,41]

We can recommend utilization of PEEP at the levels tested in this study during OLV, independently of the closed or open chest situation, since there was not any interactive effect between these two factors that could act detrimentally to the cardiac function and DO_2 in normal dogs.

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Figure 7.1 Pulmonary arterial wedge pressure for 7 clinically normal anesthetized dogs for the interaction between OLV-PEEP$_{2.5}$-PEEP$_5$ and closed-open chest ($P = 0.01$).

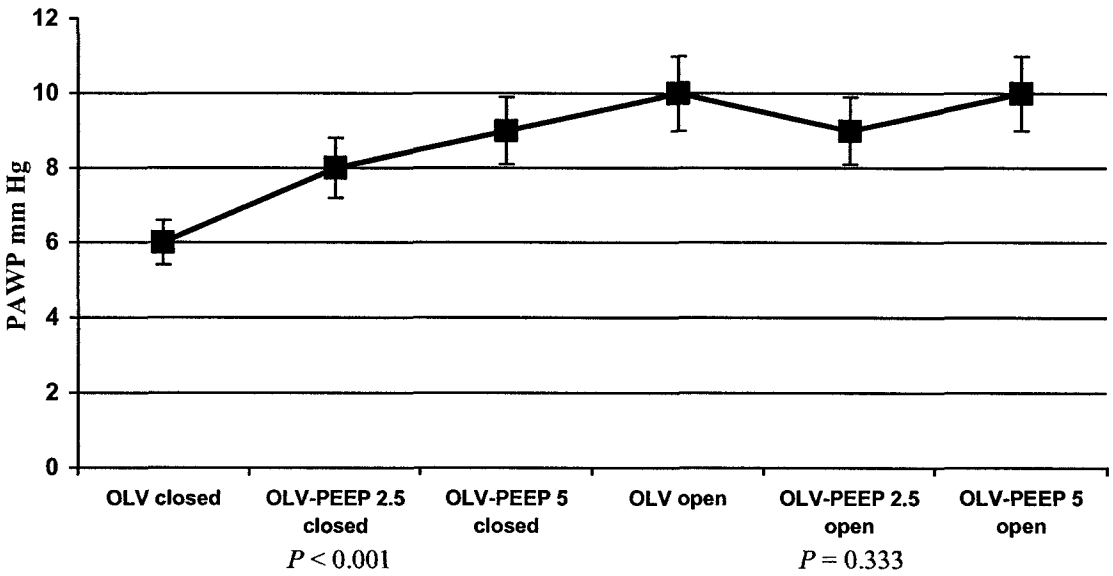

Figure 7.2 Mean pulmonary arterial pressure for 7 clinically normal anesthetized dogs for the interaction between OLV-PEEP$_{2.5}$-PEEP$_5$ and closed-open chest ($P = 0.004$).

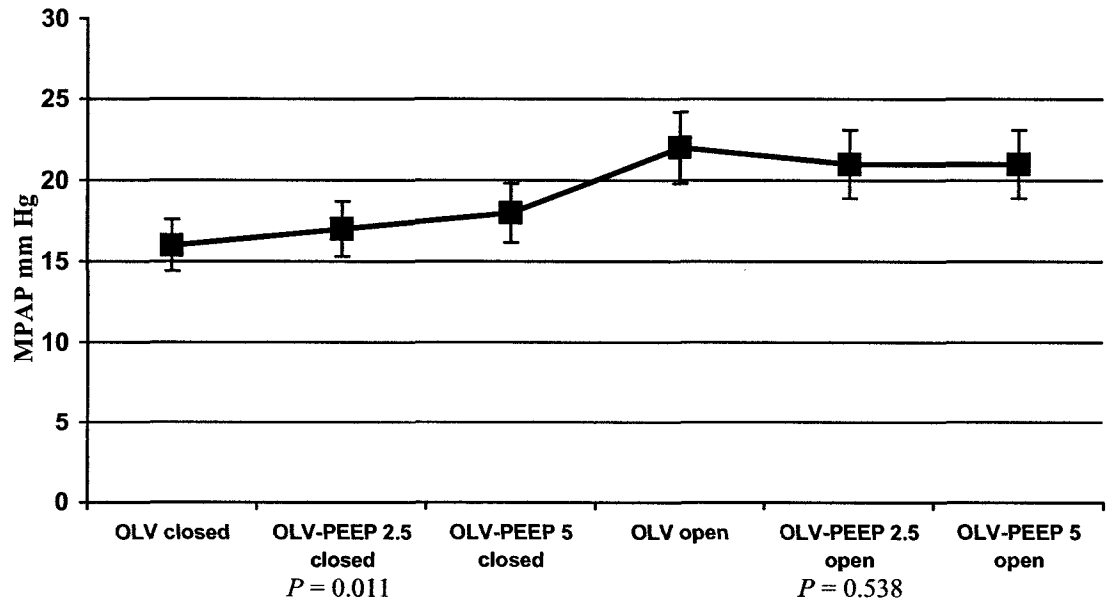

Table 7.1 Mean ± SE values for respiratory variables of 7 clinically normal anesthetized dogs for the interaction between OLV-$PEEP_{2.5}$-$PEEP_5$ and closed-open chest.

VARIABLE*	OLV WITH CLOSED CHEST			OLV WITH OPEN CHEST			*P*-value
	0 PEEP	$PEEP_{2.5}$	$PEEP_5$	0 PEEP	$PEEP_{2.5}$	$PEEP_5$	
PaO_2 (mm Hg)	170 ± 25	207 ± 26	245 ± 37	188 ± 36	208 ± 38	243 ± 38	0.809
$PaCO_2$ (mm Hg)	44 ± 2	42 ± 2	43 ± 3	44 ± 1	44 ± 1	44 ± 2	0.473
PvO_2 (mm Hg)	60 ± 3	61 ± 3	62 ± 4	58 ± 3	58 ± 3	58 ± 3	0.575
pHa	7.30 ± 0.02	7.30 ± 0.02	7.30 ± 0.03	7.30 ± 0.01	7.30 ± 0.01	7.30 ± 0.01	0.628
HCO^-_3a (mEq/L)	22.0 ± 0.4	21.0 ± 0.4	22.0 ± 0.5	22.0 ± 0.4	21.0 ± 0.3	21.0 ± 0.4	0.251
ABEa (mEq/L)	-4.1 ± 0.6	-4.9 ± 0.5	-4.7 ± 0.6	-4.9 ± 0.5	-5.2 ± 0.3	-5.0 ± 0.4	0.296
$P_{ET}CO_2$ (mm Hg)	35 ± 2	35 ± 2	36 ± 2	35 ± 1	35 ± 1	36 ± 1	0.624
SaO_2 (%)	98.6 ± 0.2	99.0 ± 0.2	99.2 ± 0.2	98.7 ± 0.3	98.8 ± 0.3	99.2 ± 0.3	0.502
SvO_2 (%)	86.4 ± 1.3	86.8 ± 1.5	86.9 ± 1.5	84.6 ± 1.6	84.6 ± 1.6	84.4 ± 1.8	0.861
* See list of abbreviations							

Table 7.2 Mean ± SE values for hemodynamic variables of 7 clinically normal anesthetized dogs for the interaction between OLV-$PEEP_{2.5}$-$PEEP_5$ and closed-open chest.

	OLV WITH CLOSED CHEST			OLV WITH OPEN CHEST			
Variable*	**0 PEEP**	**$PEEP_{2.5}$**	**$PEEP_5$**	**0 PEEP**	**$PEEP_{2.5}$**	**$PEEP_5$**	***P*-value**
SAP (mm Hg)	108 ± 6	109 ± 6	111 ± 6	113 ± 10	105 ± 6	109 ± 4	0.406
DAP (mm Hg)	57 ± 3	60 ± 3	61 ± 2	64 ± 6	58 ± 3	63 ± 3	0.195
MAP (mm Hg)	74 ± 3	76 ± 4	77 ± 3	80 ± 7	74 ± 4	77 ± 3	0.158
RAP (mm Hg)	5.0 ± 0.3	7.0 ± 0.7	7.0 ± 0.3	9.0 ± 0.7	9.0 ± 0.5	9.0 ± 0.7	0.142
PAWP (mm Hg)	6 ± 1	8 ± 1	9 ± 1	10 ± 1	9 ± 1	10 ± 1	0.010**
SPAP (mm Hg)	21 ± 1	24 ± 1	23 ± 1	28 ± 2	29 ± 2	27 ± 2	0.094
DPAP (mm Hg)	11 ± 1	12 ± 1	13 ± 1	15 ± 1	15 ± 1	15 ± 1	0.079
MPAP (mm Hg)	16 ± 1	17 ± 1	18 ± 1	22 ± 2	21 ± 1	21 ± 1	0.004**
HR (beats/min)	117 ± 4	117 ± 5	115 ± 6	119 ± 6	119 ± 6	120 ± 6	0.486
CORE BODY Temperature (C°)	36.5 ± 0.3	36.5 ± 0.3	36.7 ± 0.3	36.9 ± 0.3	37 ± 0.4	37 ± 0.4	0.601

* See list of abbreviations ** *P*-value shows a significant interaction for OLV-$PEEP_{2.5}$-$PEEP_5$ and closed-open chest at $P < 0.05$.

Table 7.3 Mean ± SE values for calculated cardiopulmonary variables of 7 clinically normal anesthetized dogs for the interaction between OLV-$PEEP_{2.5}$-$PEEP_5$ and closed-open chest.

Variable*	OLV WITH CLOSED CHEST			OLV WITH OPEN CHEST			*P*-value
	0 PEEP	$PEEP_{2.5}$	$PEEP_5$	0 PEEP	$PEEP_{2.5}$	$PEEP_5$	
CaO_2 (mL/dL)	21.6 ± 0.8	21.8 ± 0.9	22 ± 0.9	21.6 ± 0.8	21.7 ± 0.9	22 ± 0.9	0.734
Qs/Q_T (%)	30 ± 2	28 ± 1	25 ± 1	29 ± 2	27 ± 2	23 ± 1	0.301
DO_2 (mL/kg/min)	1,028 ± 136	1,105 ± 111	996 ± 144	1,227 ± 183	1,178 ± 156	1,207 ± 158	0.496
PVRI (mm Hg/L/min/m^2)	2.0 ± 0.2	2.0 ± 0.2	2.0 ± 0.3	2.0 ± 0.2	2.0 ± 0.2	2.0 ± 0.2	0.152
SVRI (mm Hg/L/min/m^2)	15 ± 2	13 ± 1	15 ± 1	13 ± 2	12 ± 1	13 ± 2	0.539
O_{2ER} (%)	12.4 ± 0.1	12.3 ± 0.1	12.5 ± 0.2	14.2 ± 0.2	14.4 ± 0.2	15.0 ± 0.2	0.882
CI (L/min/m^2)	5.1 ± 0.6	5.4 ± 0.5	4.8 ± 0.6	6.1 ± 0.9	5.8 ± 0.8	5.9 ± 0.8	0.278
V_D/V_T (%)	21 ± 2	18 ± 2	18 ± 1	22 ± 2	20 ± 1	18 ± 1	0.857
P_A-aO_2 (mm Hg)	375 ± 27	340 ± 27	301 ± 37	351 ± 35	335 ± 37	317 ± 40	0.414
PaO_2 (mm Hg)	545 ± 6	547 ± 6	546 ± 7	545 ± 5	545 ± 6	546 ± 6	0.473

* See list of abbreviations.

ENDNOTES

a. Insyte, Becton Dickinson Infusion Therapy Systems Inc, Sandy, Utah.

b. Lactated Ringer's injection, Abbott Laboratories, North Chicago, Ill.

c. PropoFlo, Abbott Laboratories, North Chicago, Ill.

d. Diazepam injection, Elkins-Sinn Inc, Cherry Hill, NJ.

e. IsoFlo, Abbott Laboratories, North Chicago, Ill.

f. Isoflurane precision vaporizer, Vetland, Louisville, Ky.

g. Ohmeda 5330 agent monitor, Datex-Ohmeda, Louisville, Colo.

h. Reusable temperature probe, Yellow Springs Instrument Co, Yellow Springs, Ohio.

i. 6% Gentran 70 and 0.9% sodium chloride injection, Baxter Healthcare Corp, Deerfield, Ill.

j. Atracurium besylate injection, Faulding Pharmaceutical Co, Elizabeth, NJ.

k. Mini Stim model MS-1, Life-Tech Inc, Houston, Tex.

l. Narkomed DA, 2-liter volume limited ventilator, North American Drager, Telford, Pa.

m. Side-stream end-tidal CO_2 sensor, model 20021, Medical Data Electronics, Arleta, Calif.

n. Wright's respirometer type PM, Ferraris Medical Inc, Holland, NY.

o. Lifescope 6, Nihon/Kohden, Tokio, Japan

p. Datex-Ohmeda ear clip pulse oxymeter sensor, Datex-Ohmeda, Louisville, Colo.

q. Opticath catheter, Abbott Critical Care Systems, Abbott Laboratories, North Chicago, Ill.

r. Arrow percutaneous sheath introducer system. Arrow International Inc, Reading, Pa.

s. CDXpress, Argon, Maxxim Medical, Athens, Tex.

t. Market, series 7000 monitor, Marquette Electronics Inc, Milwaukee, Wis.

u. Explorer oxymetry computer, Baxter Healthcare Corp, Edwards Critical-Care Division, Santa Ana, Calif.

v. IRMA blood analysis system series 2000, Diametrics Medical Inc, St Paul, Minn.

w. Arndt endobronchial blocker, Cook Critical Care, Bloomington, Ind.

x. Arndt multiport airway adapter, Cook Critical Care, Bloomington, Ind.

y. Evis bronchovideoscope, Olympus BF type 240 series, Olympus America Inc, Melville, NY.

z. Thoracic trocar sleeve, Ethicon Endo-Surgery Inc, Johnson & Johnson Healthcare Systems, Fort Worth, Tex.

aa. Fentanyl citrate injection, Abbott Laboratories, North Chicago, Ill.

bb. Duragesic, Fentanyl transdermal system, Janssen Pharmaceutical Products, Titusville, NJ.

VIII SUMMARY AND CONCLUSIONS

One-lung ventilation in clinically normal dogs with a closed thoracic cavity did not significantly affect DO_2 because despite the augmentation in Q_S/Q_T and the slight but significant decreases in PaO_2, SaO_2 and CaO_2, CI was not sufficiently changed to affect DO_2. However, the nonsignificant changes in CI and DO_2 had a very low power (0.062 and 0.142 respectively), and the fact that despite DO_2 not changing statistically but still increasing by 17% during OLV respective to TLV, leads us to be confident that DO_2 is not biologically impaired by OLV.

The use of $PEEP_{2.5}$ and $PEEP_5$ during OLV with a closed chest resulted in a significant reduction of Q_S/Q_T, compared with the baseline value during OLV without PEEP. However, the net effect of PEEP on hemodynamic and respiratory variables was that DO_2 was not significantly altered. The changes in the two factors determining DO_2, CaO_2 and CI, although not statistically significant, also had low powers (0.067 and 0.441 respectively). However, $\mathbf{O_{2ER}}$, an important variable to evaluate alterations in DO_2, was not significantly changed and had an excellent power (0.968), which confirms that there was no detrimental effect of PEEP on DO_2.

Results for interaction between TLV-OLV and closed-open chest showed a significant effect on Q_S/Q_T, PaO_2, CaO_2, and $P_A\text{-}aO_2$, but not on SaO_2. Hemodynamic parameters were not affected by the interaction. As a net result of this interaction on hemodynamic and respiratory variables, DO_2 was not significantly altered. However, it is

interesting to look at the absolute values for the results of DO_2 considering that despite the quite similar values of CaO_2 during either closed or open chest, both CI and DO_2, rose by about 20% during open chest with respect to their values during closed chest. This is important given that OLV is mainly used with open chest.

For the interaction between OLV-$PEEP_{2.5}$-$PEEP_5$ and closed-open chest, there was a significant effect of the interaction on PAWP and MPAP. There was no significant interactive effect on other hemodynamic and respiratory parameters. As a net result DO_2 was not significantly altered.

The results of these experiments suggest that despite the low power obtained for some of the important cardiopulmonary variables, the use of OLV and the levels of PEEP described here, with either closed or open chest in healthy dogs, mainly affect respiratory variables without significantly altering hemodynamic values. Therefore, OLVcan be used safely because it should not induce a reduction of DO_2, providing the circulatory variables of the patients are stable. However, additional studies are necessary to confirm these findings in diseased patients and for various ages, body positions, and conditions in which a more profound deterioration of the respiratory values is present even if the circulatory values are stable.

Similarly, we recommend use of the levels of PEEP described here during OLV, because PEEP was not detrimental to cardiac function and DO_2, and any gain in oxygenation variables may be valuable in diseased patients, even if in our healthy dogs the improvement in oxygenation did not extend to an increase in DO_2.

APPENDIX

FORMULAS USED FOR CALCULATED RESPIRATORY AND HEMODYNAMIC VARIABLES

$Cc'O_2 = ([1.36 \text{ X Hb X } 100]/100) + (0.003 \text{ X } P_AO_2)$

$P_AO_2 = (F_IO_2 \text{ X } [P_B - P_{H_2O}]) - (1.2 \text{ X } PaCO_2)$

$Q_S/Q_T = (Cc'O_2 - CaO_2)/Cc'O_2 - CvO_2)$

$CaO_2 = (1.36 \text{ X Hb X } SaO_2) + (0.003 \text{ X } PaO_2)$

$CvO_2 = (1.36 \text{ X Hb X } SvO_2) + (0.003 \text{ X } PvO_2)$

$P_A\text{-}aO_2 = P_AO_2 - PaO_2.$

$DO_2 = CO \text{ X } CaO_2 \text{ X } 10$

$CI = CO/BSA.$

$O_{2ER} = (SaO_2 - SvO_2)/SaO_2$

$PVRI = (MPAP - PAWP)/CI$

$SVRI = (MAP - RAP)/CI$

$V_D/V_T = ([PaCO_2 - P_{ET}CO_2]/PaCO_2) \text{ X } 100$

LIST OF ABBREVIATIONS

Two-lung ventilation (TLV)

One-lung ventilation (OLV)

Positive end-expiratory pressure (PEEP)

Arterial oxygen partial pressure (PaO_2)

Mixed venous blood oxygen partial pressure (PvO_2)

Arterial oxygen saturation (SaO_2)

Mixed-venous oxygen saturation (SvO_2)

Alveolar oxygen partial pressure (P_AO_2)

Alveolar-arterial oxygen partial pressure difference (P_A-aO_2)

Shunt fraction (Q_S/Q_T)

Oxygen delivery (DO_2)

Arterial carbon dioxide partial pressure ($PaCO_2$)

Arterial oxygen content (CaO_2)

Mixed-venous oxygen content (CvO_2)

End-tidal partial pressure of carbon dioxide ($P_{ET}CO_2$)

Arterial pH (pHa)

Arterial bicarbonate concentration (HCO_3^-a)

Arterial acid-base excess (ABEa)

Heart rate (HR)

Pulmonary artery wedge pressure (PAWP)

Systolic pulmonary artery pressure (SPAP)

Diastolic pulmonary artery pressure (DPAP)

Mean pulmonary artery pressure (MPAP)

Systolic arterial pressure (SAP)

Diastolic arterial pressure (DAP)

Mean arterial pressure (MAP)

Central venous pressure (CVP)

Right atrial pressure (RAP)

Carbon dioxide (CO_2)

Cardiac output (CO)

Cardiac index (CI)

Hypoxic pulmonary vasoconstriction (HPV)

Pulmonary vascular resistance (PVR)

Pulmonary vascular resistance index (PVRI)

Systemic vascular resistance index (SVRI)

Functional residual capacity (FRC)

Double-lumen endotracheal tubes (DLT)

Ventilation/perfusion (V/Q)

Pulmonary end-capillary oxygen content ($Cc'O_2$)

Hemoglobin concentration (Hb)

Inspired fraction of oxygen (FIO_2)

Barometric pressure (P_B)

Partial pressure of water vapor (P_{H_2O})

Oxygen extraction ratio (O_{2ER})

Dead space (V_D/V_T)

Body surface area (BSA)

Two and a half cm H_2O of PEEP ($PEEP_{2.5}$)

Five cm H_2O of PEEP ($PEEP_5$)

Zero cm H_2O of PEEP (0 PEEP)