The effects of dobutamine, nitroprusside, or volume expansion on cardiac output and lung water after CPPV

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Pulmonary microemboli can create an ARDS-like state in dogs (high pulmonary vascular resistance, pulmonary oedema and arterial hypoxemia). CPPV can correct the hypoxemia of pulmonary microemboli but reduces cardiac output ($\dot{Q}$) and tissue oxygenation. This paper compares the effect of improving $\dot{Q}$ by infusing volume, reducing afterload, or increasing myocardial contractility. Four groups of seven dogs were studied. All had 0.125 $g \cdot kg^{-1}$ of starch microemboli (63–74 microns) infused and then CPPV at 15 cm H_2O applied. The control group had no further treatment applied. In three other groups volume (dextran) or dobutamine or nitroprusside (NTP) was infused to return $\dot{Q}$ to the level before CPPV was applied. All treatments (volume, dobutamine and NTP) improved $\dot{Q}$ and O_2 transport. Only the volume group had a significant increase in pulmonary microvascular pressure, $Pmv = P\overline{LA} + 0.4(P\overline{PA} - P\overline{LA})$ from 2.53 ± 0.27 to 3.35 ± 0.13 kPa, $p < 0.05$. Only the volume group demonstrated a significant increase in lung water above (double) the control group as measured by a double indicator dilution technique (ETVL) and post mortem lung weights. We conclude volume infusions to improve a CPPV depressed $\dot{Q}$ may increase lung water and that better treatment would be to infuse NTP or dobutamine, thus maintaining a lower Pmv and therefore lung water. As a corollary the least CPPV should be applied to maintain adequate oxygenation and create the least need for interventions to improve $\dot{Q}$.

Key words
HEART: cardiac output; LUNG: oedema;
VENTILATION: continuous positive pressure;
SYMPATHETIC NERVOUS SYSTEM: dobutamine;
PHARMACOLOGY: nitroprusside.

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The adult respiratory distress syndrome (ARDS) is associated with an increase in pulmonary vascular resistance (PVR), pulmonary oedema and arterial hypoxemia. Pulmonary microemboli have been suggested as a cause of ARDS.[1] Continuous positive pressure ventilation (CPPV) can correct the hypoxemia of pulmonary microemboli, but reduces cardiac output ($\dot{Q}$) and tissue oxygenation.[2] The reduced $\dot{Q}$ after CPPV can be improved by infusing fluid volume.[3] We found fluid infused after CPPV did increase $\dot{Q}$ in the high PVR setting of pulmonary microemboli, but it also increased lung water.[3]

It is possible that other techniques to improve the reduced $\dot{Q}$ of CPPV (reduced afterload or increased myocardial contractility) might not increase lung water after pulmonary microemboli. This experiment compares gas exchange and haemodynamic events in a high PVR setting when the low $\dot{Q}$ associated with CPPV is treated by infusing fluid volume, reducing afterload or increasing myocardial contractility.

Methods

Animal preparation and measurements

Twenty-eight mongrel dogs weighing between 16

and 36 kg were studied. Anaesthesia was induced with pentobarbitone 30 mg·kg^{-1} IV and maintained with additional boluses of 50 mg as required. The animals breathed or were ventilated with air throughout the experiment.

In order to monitor pressures continuously the femoral artery, pulmonary artery (P_{PA}), and left atrium (P_{LA}) were catheterized.[4] Mean pressures were taken over several respiratory cycles. No correction was made for increases in pleural pressure once CPPV was applied. Arterial and mixed venous blood samples were analyzed for blood gases and haemoglobin (HB). All values were corrected for pulmonary artery blood temperature which was maintained with a heating blanket. Oxygen content was calculated. Mixed expired gases, simultaneously collected through a tracheostomy, were analyzed for O_2 and CO_2 concentrations. Using this information venous admixture (Q_S/Q_T) and pulmonary deadspace (V_D/V_T) were then calculated using standard equations.[5] Oxygen consumption was calculated using the expired gas volume, and expired O_2 and CO_2 concentrations.[5] Cardiac output, central blood volume (CBV), and lung water (ETV_L) were measured using the thermodilution double indicator technique.[6–8]

Pulmonary microvascular pressure (Pmv) was calculated as $Pmv = \overline{P_{LA}} + 0.4\,(\overline{P_{PA}} - \overline{P_{LA}})$.[10] Oxygen transport was calculated as the product of cardiac output and arterial O_2 content. Oxygen extraction was calculated as O_2 consumption/O_2 transport. All lines were kept open by flushing with normal saline, which resulted in a total infusion of 150 ml·hour^{-1} in all groups.

Glossary of terms

$\overline{P_{PA}}$	= mean pulmonary artery pressure (kPa)
$\overline{P_{LA}}$	= mean left atrial pressure (kPa)
Pmv	= pulmonary microvascular pressure (kPa)
$\dot{Q}$	= cardiac output (L·min^{-1})
CBV	= central blood volume (ml·kg^{-1})
$PaCO_2$	= arterial pressure of carbon dioxide (kPa)
PaO_2	= arterial pressure of oxygen (kPa)
B.E.	= base excess (mEq·L^{-1})
$P\bar{v}O_2$	= mixed venous partial pressure of oxygen (kPa)
CaO_2	= arterial oxygen content (ml·dl^{-1})
$S\bar{v}O_2$	= mixed venous oxygen saturation (%)
Q_S/Q_T	= shunt fraction
O_2 extraction	= oxygen consumption/oxygen transport
ETV_L	= extravascular thermal volume of the lung (lung water), ml·kg^{-1}
PETW	= pulmonary extravascular tissue weight (ml·kg^{-1})
Hb	= haemoglobin (gm %)

Double indicator dilution technique

A 2 mm OD silastic catheter containing a VECO thermistor catheter (time constant 0.12 sec) was floated into the pulmonary artery (PA) from the external jugular vein. Placement of the catheter tip just inside the pulmonary artery was determined with pressure monitoring. A 2.5 mm OD catheter containing two stainless steel electrodes for blood electrical conductivity measurements and a VECO thermistor catheter was advanced from the femoral artery to the aortic arch.[6,7] Pressures were recorded on a Beckman dynagraph type RM six channel recorder.

For each determination of ETV_L 5 ml of room temperature three per cent saline were injected into the PA. The midpoint of injection and the difference between injectate temperature in the pulmonary artery and dog blood temperature were computed. Blood was withdrawn through the aortic sensing catheter at 43 ml·min^{-1} and then immediately reinfused. Aortic blood conductivity and temperature changes were recorded.[8] Conductivity and thermodilution curves were integrated and corrected for recirculation by extrapolation to zero of the downslope exponential calculated between 80 and 40 per cent of the curve peak. Cardiac output ($\dot{Q}$) was computed using Hosie's formula of thermodilution.[9] Mean transit time (MTT) was computed by the equation:

$$MTT = \frac{\int_0^\infty t \cdot c(t)dt}{\int_0^\infty c(t)dt}$$

where c(t) is the outflow indicator concentration. Then $ETV_L = Q_T\,(MTT_T - MTT_{EC})$ where MTT_T is mean transit time of the thermal indicator and MTT_{EC} is mean transit time of the change in electrical conductivity.

A calibration factor for each thermistor was recorded over the temperature range used immedi-

ately prior to each experiment by setting the thermistors in a rapidly stirred spontaneously cooling beaker of water.

Protocol

After baseline measurements, $0.125\,g\cdot kg^{-1}$ of starch microemboli (63–74 microns in diameter) were infused as a single bolus through a large bore catheter inserted into the external jugular vein.

Thirty minutes after embolization, measurements were taken. The results of these measurements will be identified as "Embolus."

CPPV at 15 cm H_2O end tidal pressure was then applied and measurements were repeated after 30 minutes and labelled "CPPV 15." Ventilation was achieved with a tidal volume of $12\,ml\cdot kg^{-1}$ and frquency altered to achieve a $PaCO_2$ of 5.32 kPa (40 mmHg). Paralysis was induced with 0.2 $mg\cdot kg^{-1}$ of pancuronium.

The animals were then divided into four groups according to treatment applied:

1 *Control* – in seven dogs, while CPPV was applied, measurements were repeated every 30 minutes for three hours.
2 *Volume* – in seven dogs, while CPPV was applied, ten per cent dextran 40 in normal saline was infused until $\dot{Q}$ was returned to the "embolus value," and then infusion was stopped. The volume of dextran infused was 464 ± 24 ml.
3 *Dobutamine* – in seven dogs, while CPPV was applied, dobutamine was infused to return Q to the "embolus value." While we always could increase Q by infusing dobutamine we were not always successful in returning Q to the "embolus" value. In these dogs our highest dose of dobutamine was $40\,\mu g\cdot kg^{-1}\cdot min^{-1}$. The mean final dose of dobutamine was $30\,\mu g\cdot kg^{-1}\cdot min^{-1}$.
4 *Nitroprusside* – in seven dogs, while CPPV was applied, nitroprusside (NTP) was infused at $10\,\mu g\cdot kg^{-1}\cdot min^{-1}$. This resulted in a reduced arterial pressure. With NTP running, ten per cent dextran 40 in normal saline was then infused to return Q to the "embolus value." The volume of dextran infused was 198 ± 50 ml.

Measurements in all groups of dogs were repeated every 30 minutes for three hours while CPPV and treatment was continued.

At the end of the experiment, the animals were killed with an intravenous injection of KCl, and the lungs excised. The extravascular lung water was then determined using a gravimetric method to measure pulmonary extravascular tissue weight (PETW).[6] This technique utilizes Hb to determine residual lung blood volume which is subtracted from total lung weight.

Animals were humanely cared for, in accordance with the recommendations of the Canadian Council on Animal Care, the requirements under "The Animals for Research Act, R.S.O. 1970" and the regulations of the University Animal Care Committee, University of Toronto.

Statistical anlaysis of the results within groups was carried out using a two-way analysis of variance. Comparisons between groups were made using a one-way analysis of variance. Dunnett's and Tukey's tests were used for multiple comparisons between means. $P < 0.05$ was considered significant.[11] Only significant changes will be discussed. Data are reported as mean ± SEM.

Results

There were no significant diferences between the four groups up to the time drug or volume treatment was applied. In 28 dogs 30 minutes after emboli, $\overline{PA}$ increased from 2.4 ± 0.09 to 4.4 ± 0.23 kPa* ($p < 0.001$); PaO_2 fell from 11.2 ± 0.3 to 6.9 ± 0.4 kPa ($p < 0.001$); Qs/QT increased from 14 ± 1 to 43 ± 3 per cent ($p < 0.001$); and $\dot{Q}$ fell from 3.5 ± 0.2 to 2.9 ± 0.2 L/min ($p < 0.005$). There was a small but significant increase in lung water, from 13.6 ± 0.6 to 15.6 ± 0.9 $ml\cdot kg^{-1}$ ($p < 0.005$). As in our previous results[2,3] CPPV at 15 cm H_2O after emboli increased PaO_2 from 6.9 ± 0.4 to 9.8 ± 0.3 kPa ($p < 0.001$) and reduced Qs/QT from 43 ± 3 to 14 ± 2 per cent ($p < 0.001$), but because $\dot{Q}$ was reduced from 2.9 ± 0.2 to 1.8 ± 0.1 $L\cdot min^{-1}$ ($p < 0.001$), O_2 transport fell from 435 ± 28 to 319 ± 22 ml O_2/min ($p < 0.001$).

Haemodynamic effects of drug or volume treatments

$\dot{Q}$ remained low after CPPV in the control group (Figure 1). Dobutamine, NTP and volume treatments increased $\dot{Q}$ above the control group value at the same time; however, in the dobutamine group $\dot{Q}$ remained significantly lower than the embolus value at the first measurement after dobutamine was infused (Figure 1). In the volume group, volume

*To convert from kPa to mmHg multiply value by 7.5.

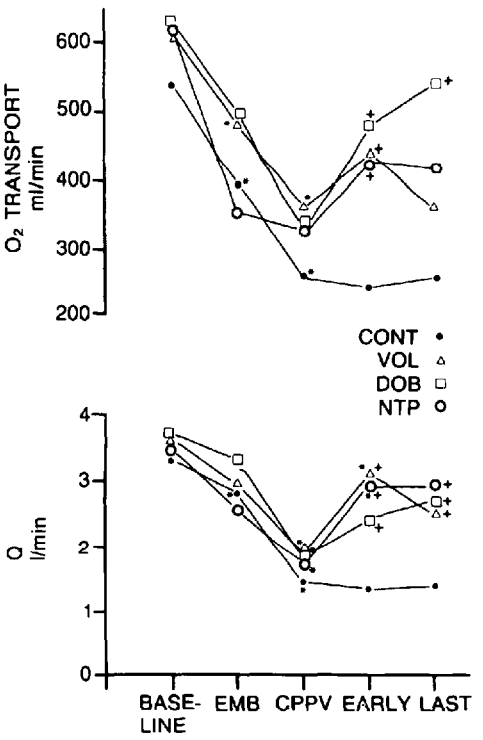

FIGURE 1 Cardiac output and oxygen transport in the four groups of dogs during the control period (BASELINE), after emboli (EMB), once CPPV was applied (CPPV), 30 min after treatment (volume [VOL], dobutamine [DOB] or nitroprusside [NTP]) was applied (EARLY), and at the end of the experiment (LAST). *Indicates a significant difference from the preceding value. +Indicates a significant difference from the control group.

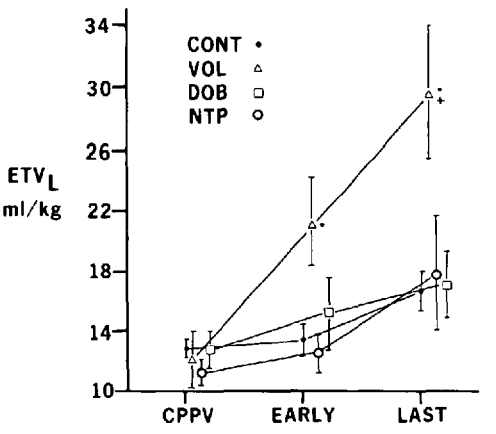

FIGURE 2 Lung water measurements (ETV_L) in the four groups at the indicated times. See Figure 1 for abbreviations. *Indicates a significant difference from the previous value, + indicates a significant difference form all other groups.

infusion resulted in a significant increase in $\overline{P_{PA}}$ (4.5 ± 0.3 to 5.5 ± 0.9 kPa), $\overline{P_{LA}}$ (1.2 ± 0.3 to 1.9 ± 0.1 kPa), and Pmv (2.5 ± 0.3 to 3.3 ± 0.1 kPa). These pressures did not increase significantly in the NTP or dobutamine groups after treatment. Central blood volume (CBV) increased with volume infusion 12 ± 2 to 17 ± 2 ml·kg^{-1}, $p < 0.025$, but remained unchanged with NTP or dobutamine infusions. Mean arterial pressure increased with volume infusion (16.5 ± 0.7 to 19.2 ± 1.2 kPa, $p < 0.05$), but was unchanged by NTP or dobutamine infusion.

Lung water effects of treatments

While there was a tendency for lung water to increase in all groups of dogs by the end of the experiment (mean values increased) only the volume group of dogs showed a significant increase at the early and last treatment value (Figure 2). By the end of the experiment lung water was twice as high in the volume group as in the other three groups (Figure 2). When the last ETV_L is plotted against PETW, a good relationship emerges, which is not significantly different between groups (Figure 3). The ratio of last ETV_L/PETW was not different between groups and the mean value for all dogs was 1.19 ± 0.06.

Gas exchange effects of treatments

After treatment was applied PaO_2, $PaCO_2$, Q_S/Q_T and V_D/V_T were not significantly changed in any group.

Tissue oxygenation effects of treatments

Haemoglobin (Hb) was significantly diluted by the infusion of dextran in both the volume (15.3 ± 0.8 to 10.9 ± 0.6 gm per cent, $p < 0.05$) and NTP groups (13.9 ± 0.5 to 11.6 ± 0.5 gm per cent, $p < 0.05$). While there was a tendency for Hb to increase in both control and dobutamine groups it only reached significance in the dobutamine groups (14.2 ± 0.4 to 16.0 ± 0.4 gm per cent, $p < 0.05$). This effected CaO_2 so that it was significantly reduced after volume was infused into the volume group (19.1 ±

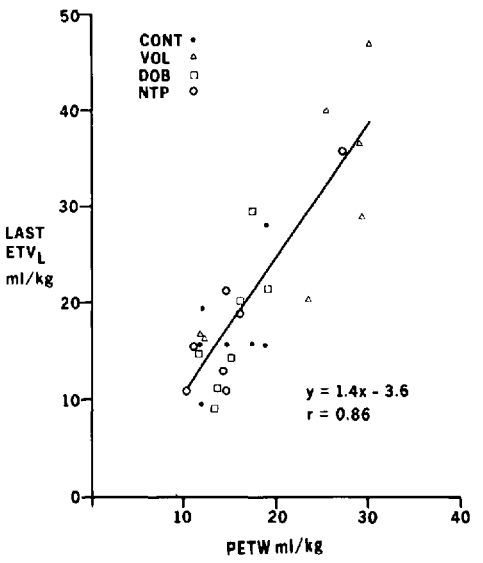

FIGURE 3 Last ETVL (lung water) measurement plotted against the post mortem weighing technique for lung water (PETW) in the four groups of dogs.

1 to 14.2 ± 0.7 ml O_2/100 ml, $p < 0.05$) and the NTP group (17.4 ± 1 to 14.5 ± 0.8 ml O_2/100 ml, $p < 0.05$). The effect of the changes in CaO_2 and $\dot{Q}$ on O_2 transport was a significant increase in all treatment groups when compared to the control groups (Figure 1). O_2 consumption increased after volume was infused in the volume group (104 ± 18 to 129 ± 12 ml·min^{-1}, $p < 0.05$) and after dobutamine infusion (119 ± 11 to 154 ± 30 ml·min^{-1}, $p < 0.05$). O_2 consumption was not changed in the control or NTP groups. O_2 extraction was not changed significantly, although mean values after treatment were lower in all treatment groups than in the control group.

While mixed venous O_2 saturation ($S\bar{v}O_2$) and $P\bar{v}O_2$ were higher in all treatment groups than in the control group, only in the volume group did the treatment result in a statistically significant increase; $P\bar{v}O_2$ 5.2 ± 0.1 to 6.1 ± 0.1 kPa, $p < 0.05$, $S\bar{v}O_2$ 69 ± 5 to 76 ± 2 per cent, $p < 0.05$.

A progressively developing metabolic acidosis was seen in the control group (last BE −11 ± 1 mEq·L^{-1}) and the dobutamine group (last BE −10 ± 3 mEq·L^{-1}). In contrast, the volume group (last BE −6 ± 1 mEq·L^{-1}) had a significantly smaller base deficit than the control group by the end of the experiment. The last BE was not significantly different from the control group in either the dobutamine (last BE −10 ± 1 mEq·L^{-1}) or NTP groups (last BE −8 ± 1 mEq·L^{-1}).

Discussion

The findings in this study reaffirm our previous findings that: (a) CPPV improves PaO_2 and Qs/Qt after pulmonary microemboli;[2,3] (b) CPPV reduces $\dot{Q}$ in this high PVR setting;[2,3] (c) the resultant effect of CPPV after pulmonary emboli is not beneficial since tissue oxygenation is reduced (decreased O_2 transport and consumption, worsening metabolic acidosis);[2] (d) when volume is infused to correct the CPPV reduced $\dot{Q}$, tissue oxygenation is improved (increased O_2 transport, O_2 consumption, $P\bar{v}O_2$, $S\bar{v}O_2$ and reduced metabolic acidosis) but a large increase in lung water results.[3]

CPPV decreases $\dot{Q}$, most likely by decreasing left ventricular preload.[12,13] There is a controversy over the mechanism(s) involved. This controversy is probably created by difficulties in accurately measuring pericardial and therefore transmural cardiac pressures.[13,14] This study was not designed to determine the cause of the reduced $\dot{Q}$ after CPPV, but to determine if a treatment other than volume infusion might (a) increase $\dot{Q}$ and (b) tissue oxygenation without increasing lung water in a high PVR setting.

(a) *Increase $\dot{Q}$*

All treatments (volume, NTP and volume, dobutamine) increased $\dot{Q}$ above the control group. By using NTP, $\dot{Q}$ could be returned to the pre-CPPV value by infusing less volume of dextran (198 ± 50 ml) than in the volume group (464 ± 24 ml). Dobutamine did not initially return $\dot{Q}$ to the pre-CPPV value and very high doses (30 μg·kg^{-1}·min^{-1}) were required to achieve these results. Although this was not done, perhaps an infusion of volume in small amounts similar to the NTP group could have improved the dobutamine results with lower doses of dobutamine required, since mean PLA was reduced by infusing dobutamine ($\bar{P}LA$ decreased from 1.2 to 1.1 kPa, NS).

(b) *Tissue oxygenation:*

Oxygen transport was improved in all groups; however, other indices of tissue oxygenation were

not as well differentiated. Volume infusion resulted in the only significant improvements in $P\bar{v}O_2$, $S\bar{v}O_2$ and last BE over the control group. While mean values for $P\bar{v}O_2$ and $S\bar{v}O_2$ were improved dobutamine and NTP groups did not demonstrate a statistically significant improvement in these measurements. O_2 consumption increased the most in the dobutamine group (119 ± 11 to 154 ± 30 $ml \cdot min^{-1}$, $p < 0.05$). These animals were all paralysed; therefore, the increased O_2 consumption was probably due to an increased myocardial O_2 demand created by the high doses of dobutamine (O_2 consumption in the myocardium can increase six-fold and is compatable with the increase of 35 $ml \cdot min^{-1}$ seen in the dobutamine group). This increased oxygen consumption and the continued fall in base excess in the dobutamine group would indicate that tissue O_2 requirements were not being met. Therefore these high doses of dobutamine were not beneficial. In a clinical setting perhaps lower doses of dobutamine and some volume would be beneficial (as in the NTP group).

$\dot{Q}$ and oxygen transport to tissues were increased in all treatment groups, but the volume group was the only group to increase lung water significantly (Figure 2). We used two techniques to measure lung water. The ETVL technique requires lung perfusion in order to measure lung water. Obviously emboli prevent lung perfusion, but if the emboli are small enough (and therefore unperfused areas are small) the thermal indicator may diffuse far enough to still accurately measure lung water.[8] To assess this accuracy we compared ETVL results to a post mortem weighing technique (PETW) and found a good comparison (Figure 3). The ratio of ETVL/PETW was not significantly different between groups. Thus emboli of the size used in this experiment did not decrease the accuracy of the ETVL measurement. When the groups were compared using ETVL or PETW the volume group had a significant increase in lung water which was not seen in the other three groups. While all three treatments increased $\dot{Q}$ and tissue oxygenation indices after CPPV, NTP and dobutamine were effective in preventing the increase in lung water seen in the volume group.

It is important to consider why volume infusion increased lung water so dramatically, while dobutamine and NTP did not. Starling's law states increases in intravascular hydrostatic pressures should increase lung water.[15] $P\overline{PA}$, Pmv and $P\overline{LA}$ were significantly increased only in the volume group. In the dobutamine group mean $P\overline{LA}$ fell (1.2 ± 0.3 to 1.1 ± 0.1 kPa, NS) while mean $P\overline{PA}$ rose (4.8 ± 0.5 to 5.1 ± 0.8 kPa, NS) resulting in an unchanged Pmv of 2.7 ± 0.1 kPa. The tendency for $P\overline{LA}$ to fall after dobutamine probably resulted from an increased myocardial contractility. The statistically insignificant increase in the $P\overline{PA}$ was also seen in the NTP group (4.5 ± 1.3 to 4.9 ± 1.2 kPa, NS) often before the small amount of volume was infused. A rise in $P\overline{PA}$ when a vasodilator (NTP) is used probably results when the increased $\dot{Q}$ is forced through an obstructed (pulmonary microemboli induced) and therefore non-compliant pulmonary vascular bed. The NTP group did not increase $P\overline{LA}$ (1.7 ± 0.1 to 1.9 ± 0.1 kPa, NS) and the final effect on Pmv (2.7 ± 0.4 to 3.1 ± 0.3 kPa, NS) was therefore small. If the pulmonary microemboli have created an increase in pulmonary capillary permeability even the small increases in pulmonary intravascular hydrostatic pressure seen in the volume group will lead to large increases in lung water since extravascular lung water accumulation becomes very sensitive to even small hydrostatic pressure changes.[16] Pulmonary intravascular pressures were not increased in the other three groups so lung water did not increase (Figure 2). Since oedema fluid may leak through large as well as small vessels[17,18] the significant increase in all three pressures (PPA, Pmv, and PLA) seen in the volume group, and prevented by increasing myocardial contractility (dobutamine) and reducing afterload (NTP), probably had an important role in creating a doubling of lung water in the volume group. However, other factors may also play a role, for when $P\overline{PA}$, $P\overline{LA}$ or Pmv are plotted against ETVL a significant relationship does not emerge. Several explanations are possible. The first is the role played by time. We have found that sudden increases in pulmonary hydrostatic pressure do not result in a linear increase in pulmonary oedema.[19] Oedema accumulates slowly at first and more quickly later, at the same hydrostatic pressure. Depending where each animal is placed on this curve the same pressure would give very different lung water results regardless of the fact that all experimental groups were studied for the same time. Secondly, pulmonary microemboli may create an increase in capillary permeability. While

Starling's law would still function, the same increase in pulmonary vascular pressures would result in different amounts of lung water depending on capillary permeability.

Since we are interested in quantitative changes in lung water induced by different treatments, the treatments must achieve comparable end points. We chose $\dot{Q}$ as our end point since CPPV reduces $\dot{Q}$ and this reduces tissue oxygenation. Volume infusions are highly successful in improving Q and the parameters of tissue oxygenation that we measured. There are no significant differences between the volume and NTP groups when $\dot{Q}$ and tissue oxygenation parameters were compared indicating these two groups are comparable. There are no significant differences between the dobutamine and volume groups when $\dot{Q}$ is compared but high doses of dobutamine are required and initially did not return $\dot{Q}$ to the embolus value. Dobutamine increased the O_2 consumption and the base deficit suggesting the increased myocardial O_2 demand was detrimental. While the three treatment groups have comparable $\dot{Q}$ the metabolic acidosis and the low $P\bar{E}_A$ after dobutamine (1.1 ± 0.2 kPa) suggest that some fluid infused in the dobutamine group (as in the NTP group) might reduce the high dose of dobutamine used, the metabolic acidosis, and our inability to immediately correct Q with dobutamine.

Gas exchange (PaO_2, $PaCO_2$, Qs/Q_T, V_D/V_T) was not altered by any of the treatments applied. In the volume group of dogs shunting did not increase with the pulmonary oedema because alveoli were held open with the CPPV applied.[20] The fact that increased shunting did not occur after treatments were applied (even in the face of an increase in $P\bar{A}$) again refutes the existance of right to left cardiac or pulmonary arterio-venous anastomoses as the cause of hypoxemia after pulmonary emboli in this dog model. Diffusion defects for O_2 have also been suggested as a cause of hypoxemia after pulmonary microemboli since lung transit time is decreased when the entire $\dot{Q}$ goes through a smaller number of vessels. CPPV could improve shunting by reducing Q and so increase time for O_2 to diffuse into blood. This experiment refutes these arguments since Q was improved while on CPPV using three different mechanisms, and yet shunt did not increase. Cardiac output reductions induced either mechanically or pharmacalogically in dogs are associated with decreased Qs/Q_T.[21] In this experiment when Qs/Q_T increased from 14 ± 1 to 43 ± 3 per cent ($p < 0.001$) $\dot{Q}$ fell from 3.5 ± 0.2 to $2.9 \pm 0.2\,L \cdot min^{-1}$ ($p < 0.005$) after emboli. The increases in $\dot{Q}$ after treatment did not alter Qs/Q_T. Therefore cardiac output chnges have not created Qs/Q_T changes in this experiment. Since NTP is known to reduce hypoxic pulmonary vasoconstriction (HPV)[22,23] these data suggest HPV did not exist after the high pulmonary vascular pressures of pulmonary microemboli. Our data support ventilation/perfusion (V/Q) abnormalities as the cause of arterial hypoxemia after emboli. These V/Q mismatches may be created by shifts in perfusion from normal lung that has been embolized to poorly ventilated, hypoxic, and therefore unembolized lung.[24,25] This increased perfusion to hypoxic lung after emboli can be matched with increased ventilation when CPPV is applied thus improving PaO_2 and shunting.

These data suggest that the reduced $\dot{Q}$ and O_2 transport created by CPPV in a high PVR setting should not be corrected by infusing volume (even though decreased left ventricular preload may be the problem). To infuse this volume will create pulmonary oedema.[3] A better solution appears to be to infuse small volumes of fluid and then reduce pulmonary vascular pressures either by reducing afterload (e.g. NTP) and/or by increasing myocardial contractility (e.g. dobutamine). Which of these is chosen should depend on the state of the myocardium and whether HPV is thought to exist (when NTP may create increased shunting).[22,23] Of course if lower levels of CPPV can be applied and an adequate oxygenation achieved the need and therefore complications of all of these interventions may be reduced.

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Résumé

Les microembolies pulmonaires peuvent créer chez les chiens un état identique au syndrome de détresse respiratoire de l'adulte (résistance vasculaire pulmonaire élevée, œdème pulmonaire et hypoxémie artérielle). La ventilation à pression positive continue peut corriger l'hypoxémie dû aux microembolies pulmonaires mais réduit le débit cardiaque ($\dot{Q}$) et l'oxygénation tissulaire. Cette étude compare les effets d'une amélioration du débit cardiaque ($\dot{Q}$) par la perfusion de volume, la réduction de la post-charge ou l'augmentation de la contractilité myocardique. Quatre groupes de sept chiens chaque, ont été étudiés. Tous ont reçu 0.125 $g \cdot kg^{-1}$ de particules d'amidon (63–74 microns) en perfusion et une ventilation à pression positive continue à 15 cmH_2O. Pour le groupe contrôle aucun traitement ne fut appliqué. Dans les trois autres groupes du volume (dextran) ou dobutamine ou nitroprussiate (NTP) a été perfusé afin de retourner le débit cardiaque ($\dot{Q}$) au niveau initial avant l'application de ventilation à pression positive continue. Tous les traitements (volume, dobutamine et NTP) ont amélioré le débit cardiaque ainsi que le transport d'oxygène. Seul le groupe "volume" a démontré une augmentation significative dans la $Pmv = P\overline{LA} + 0.4(P\overline{PA} - P\overline{LA})$ de 2.53 ± 0.27 à 3.35 ± 0.13 kPa, $p < 0.05$. Seul le groupe traité par du volume a démontre une augmentation significative de l'eau pulmonaire qui a doublé par rapport au contrôle tel que mesuré par la technique de dilution à double indicateur (ETV_L) et la pesée des poumons post-mortem. On conclut que la perfusion de volume afin d'améliorer un débit cardiaque déprimé suite à la ventilation à pession positive continue peut augmenter l'eau pulmonaire. Un meilleur traitement serait l'administration de nitroprussiate ou de dobutamine afin de maintenir un Pmv bas et ainsi empêcher la rétention de l'eau dans le poumon. Comme corollaire on devra utiliser avec précaution la ventilation à pression positive continue pour maintenir une bonne oxygénation tissulaire, afin de ne point être obliger de créer le besoin d'altérer le débit cardiaque.