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The Effect of Peep-ventilation on Cardiac Function in Closed Chest Pigs

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ABSTRACT

Objective: Does ventilation with positive end-expiratory pressure (PEEP) depress myocardial contractility?

Design: Ten piglets were anaesthetized and prepared for the measurement of cardiac output (SV) and right (MRAPtm) and left (MLAPtm) mean transmural atrial pressure, the latter serving as indices of preload. 500 ml of autologous blood was re-transfused during intermittent positive pressure ventilation without PEEP (IPPV) and continuous positive pressure ventilation with 15 cm H_2O PEEP (CPPV).

Measurements and results: Right and left ventricular function curves were drawn by plotting MRAPtm and MLAPtm respectively versus the corresponding strokevolumes before and after re-transfusion. Similar inclinations were obtained during IPPV and CPPV on either side of the heart.

Conclusions: Although the ventricular function curves during IPPV and CPPV covered partially different preload levels, the results suggest that CPPV i.e. PEEP does not affect myocardial contractility.

INTRODUCTION

Mechanical ventilation with positive end-expiratory pressure (PEEP) is commonly utilized to improve arterial oxygenation during pulmonary dysfunction. One well known side effect to this ventilatory mode is a decrease in cardiac output (CO). As the oxygen transport depends not only on the arterial oxygenation but also on the blood flow, the decrease in CO restricts the use of PEEP.

In every situation it is therefore important to find the PEEP level that results in the best oxygen transport, i.e. optimal PEEP (8, 11, 30). Hence, methods which restore the impaired CO during PEEP-ventilation are of obvious clinical value.

One example of such a method is the restoration of PEEP-induced decline in venous return (VR) (4, 11, 23, 25) by volume expansion (18, 22). The utility of this measure is, however, limited because of the risk of fluid overload (23).

Some reports suggest that part of the decrease in CO during PEEP is due to myocardial depression mediated either humorally (5, 9, 15) or through a neural pathway (2, 27). Presumably, if the mediator could be identified, it would also be possible to find a blocker. This concept has in fact been explored by Edmonds et al (6), Dunham et al (5) and Sunahara et al (29).

Some other reports refute the existence of myocardial depression during PEEP (12, 16, 17, 23, 24, 26). In fact, Prewitt et al (20) have speculated that PEEP might even improve ventricular performance!

The diverging opinions on this matter lead us to design an experimental model to study myocardial function during PEEP-ventilation in the pig.

MATERIAL AND METHODS

Animals and anaesthesia

This study was approved by the Animal Ethics Committee of the Uppsala University. Ten pigs of Swedish native breed, 20-25 kg, 10-12 weeks old and of both sexes were used. Anaesthesia was induced with pentobarbital (Mebumal® Vet, ACO), 25 mg/kg intravenously (i.v.). To avoid salivation, atropine 0.5 mg, was given (i.v.). Anaesthesia was maintained by a continuous infusion of methomidate (Hypnodil®, Jansen Pharmaceutica) 7.5 mg/kg/min. Pancuronium bromide (Pavulon®, Organon), 0.18 mg/kg/min i.v., was used as the muscle relaxant. Glucose in saline (Rehydrex®, Pharmacia) 15 ml/kg/h was given for hydration.

The pigs were placed on their back, tracheotomized and connected to a volume-controlled ventilator (Servo Ventilator 900C, Siemens) set to 30 breaths/minute. Ventilation was given with oxygen in air (FiO_2 0.3) except during the surgical preparation when nitrous oxide in oxygen was used. Minute volumes were adjusted to maintain a stable $PaCO_2$ throughout the experimental period.

Surgical procedures

In the right carotid artery a polyethylene catheter was inserted and the tip positioned in the aortic arch. Three polyethylene catheters were inserted in the left external jugular vein with the tips located in the superior vena cava.

A balloon-tipped, thermistor-probed, 7F, Swan-Ganz catheter was positioned in the pulmonary artery.

A left-sided lateral thoracotomy was performed. The pericardium was opened widely over the pulmonary artery and over the apex. A polyethylene catheter was placed in the left atrium.

A latex rubber balloon (length 10 cm, perimeter 3.6 cm) connected to a polyethylene tubing (PP 240) was placed into the pleural space lateral to the heart. The thoracic cage was then closed and a thoracic drain, with continuous suction applied, was left in situ.

Measurements

In each animal mean arterial pressure (MAP), mean right (MRAP) and mean left atrial pressure (MLAP) as well as mean pulmonary arterial pressure (MPAP) were measured by connecting the catheters to appropriate pressure transducers (EMT34, Siemens-Elema, Sweden). The zero reference level was 8 cm below the sternum.

Mean pleural pressure (MPPL) was measured with the latex-rubber balloon connected to a pressure transducer (EMT34, Siemens-Elema, Sweden) via the polyethylene catheter. The latex-rubber balloon was emptied and then filled with 2.0 ml of air before each measurement.

All signals were amplified (EMT311, Siemens- Elema, Sweden) and recorded on a multichannel ink-jet writer (Mingograf 800, Siemens- Elema, Sweden). Mean pressures were obtained by electronic dampening of the signals.

Heart rate (HR) was calculated from the arterial pressure recording.

Cardiac output was determined by the thermodilution technique using a computer device (3750 Cardiovascular Instruments Ltd, England). A bolus of 5 ml saline at room temperature was injected by means of an automatic syringe pump (ATI1 Ulab, Sweden) starting at end-expiration. The mean value of five determinations was used.

Experimental protocol

After preparation, the animals were allowed to stabilize for 45 minutes at intermittent positive pressure ventilation without PEEP (IPPV). After this period they were heparinized, 1500 IU i.v.. 500 ml of blood was collected in a blood bag via a caval vein catheter, and mixed with 1250 IU of heparin. The blood loss was substituted with 500 ml of 0.9% saline solution (Ringerdex®, Pharmacia, Sweden).

After another 15 minutes of stabilization a set of baseline measurements were recorded. Thereafter, 500 ml of the saved blood was delivered through a caval vein catheter at a rate of 100 ml per minute by means of a peristaltic roller pump (Multiperpex 2115, LKB, Sweden). A new set of measurements were recorded. After this, 500 ml of blood was again withdrawn and the animals were allowed to rest for 30 minutes. Measurements was also made before and after reftransfusion during continuos positive pressure ventilation with 15 cm H_2O of PEEP (CPPV).

The order of the two ventilation modes was alternated in every other pig.

Abbreviations, calculations and statistical arrangements

The abbreviations and formulae used for derived variables are presented in Table 1.

Mean values for the different variables were calculated from the different measurement periods. In Tables 2 and 3 we have stated mean values ± 1 SD and in Figures 1 and 2 mean values.

Statistical tests were performed using Student's t-test between groups for paired observations. Statistical significance was considered to be $p < 0.05$, and is represented by an asterisk (*).

Table 1. Abbreviations, formulae and units for the various hemodynamic variables.

HR	Heart rate, beats/minute.
MAP	Mean arterial pressure, mmHg.
MPAP	Mean pulmonary arterial pressure, mmHg.
MPPL	Mean pleural pressure, mmHg.
MLAPtm	Mean transmural left atrial pressure, (MLAP-MPPL), mmHg.
MRAP	Mean right atrial pressure, mmHg.
MRAPtm	Mean transmural right atrial pressure, (MRAP-MPPL), mmHg.
CO	Cardiac output, litres/minute.
SV	Stroke volume, (CO*1000/HR), ml/beat.
PVR	Pulmonary vascular resistance, 0.133*(MPAP-MLAP)*1/CO*60, 10^6*N*s*m^{-5}. The pressures given in mmHg.

RESULTS

There was a significant increase in heart rate (HR), mean pulmonary arterial pressure (MPAP) and mean pleural pressure (MPPL) by 22 ± 13 beats/min, 5.0 ± 6.7 mm Hg (0.67 ± 0.89 kPa) and 5.3 ± 1.2 mm Hg (0.70 ± 0.16 kPa), respectively, when PEEP ventilation was applied before volume loading. However, mean arterial pressure (MAP) remained unchanged. During PEEP ventilation cardiac output (CO) and stroke volume (SV) also decreased significantly by 29 % and by 38%, respectively. There was a significant decrease in transmural filling pressures for the left (MLAPtm) and the right (MRAPtm) atrium by 1.6 ± 1.7 mm Hg (0.21 ± 0.23 kPa) and 1.5 ± 1.5 mm Hg (0.20 ± 0.20 kPa), respectively, and a significant increase in the pulmonary vascular resistance (PVR) by 59 %.

The effect of volume loading during the two ventilation modes was as expected and almost identical. During IPPV there was a significant decrease in HR by 29±17 beats/min and increase in MAP, MPAP, MLAPtm and MRAPtm by 32±14 mm Hg (4.26±1.86 kPa), 17.8±5.2 mm Hg (2.37±0.69 kPa), 5.2±1.5 mm Hg (0.69±0.20 kPa) and 4.0±1.2 mm Hg (0.53±0.16 kPa), respectively. The corresponding changes, which were also statistically significant during PEEP-ventilation, were 37±13 beats/min, 31±18 mm Hg (4.12±2.39 kPa), 9.2±4.2 mm Hg (1.22±0.56 kPa), 3.2±1.2 mm Hg (0.43±0.16 kPa) and 2.7±0.9 mm Hg (0.36±0.12 kPa), respectively. There was a significant increase in the SV during volume loading in both ventilation modes by 85% during IPPV and by 92% during CPPV.

In Fig.1 the response to volume loading has been illustrated by SV as a function of MLAPtm during IPPV and CPPV, respectively, the slopes during both ventilation modes are identical. Fig.2 demonstrates the corresponding plot of SV as a function of MRAPtm, also with identical slopes during both ventilation modes. The plottings represent a variety of ventricular function curves.

When comparing the two ventilation modes after volume loading, a significantly higher HR was noticed during CPPV while MAP and MPAP were unchanged. Both mean left (MLAP) and mean right (MRAP) atrial pressures were higher during PEEP-ventilation with a difference of 1.7±1.1 mm Hg (0.23±0.15 kPa) and 2.5±1.1 mm Hg (0.33±0.15 kPa), respectively. On the contrary, the corresponding transmural pressures MLAPtm and MRAPtm were depressed by 3.6±1.8 mm Hg (0.48±0.24 kPa) and 2.9±1.5 mm Hg (0.39±0.20 kPa), respectively, during PEEP-ventilation. CO and SV were significantly lower during CPPV by 0.96±0.28 l/min and 10.9±5.6 ml/beat, respectively.

DISCUSSION

The level of PEEP (15 cm H_2O) in our study was chosen in order to attain marked effects on cardiac output (CO) and yet maintain homeostasis. Thus the substantial decline in stroke volume (38%) on application of PEEP was well tolerated by all animals as indicated by an undisturbed acid-base balance.

Another effect of PEEP was the increase in heart rate (HR), supporting that PEEP increases the activity of the sympathetic nervous system (3, 28). With respect to the insignificant drop in the mean arterial pressure (MAP) it would seem that the increase in HR was triggered by some other mechanism than an unloading of the baroreceptors (7). However, considering that PEEP acts to decrease aortic arch transmural pressure, an unloading of the intrathoracic baroreceptors may still have occurred.

Theoretically, changes in HR may influence stroke volume (SV) by setting the time for diastolic filling. We believe, however, that the increase in HR from 147±16 to 169±19 as was seen on application of PEEP could be disregarded in this respect (1). The same reasoning applies to the decrements in HR on volume loading.

Table 2. Hemodynamics during intermittent positive pressure ventilation without (IPPV) and with 15 cm H_2O PEEP (CPPV) before and after re-transfusion of 500 ml shed blood. Parameters and units according to Table 1. Mean values ±SD, n=10. Statistically significant differences between IPPV and CPPV before as well as after volume loading are denoted by asterisks (*). Statistically significant differences before and after volume loading during IPPV and CPPV, respectively, are denoted by $. One symbol= p<0.05, two symbols= p<0.01 and three symbols= p<0.001

	IPPV		CPPV	
	Before vol.load	**After vol.load**	**Before vol.load**	**After vol.load**
HR, beat/min	147±16	118±26 $$$	169±19 ***	132±14 $$$ *
MAP, mmHg	77±8	109±17 $$$	70±16	100±10 $$$
(kPa)	(10.2±1.1)	(14.5±2.3)	(9.3±2.1)	(13.3±1.3)
MPAP, mmHg	16.6±5.4	34.4±7.0 $$$	21.6±6.0 *	30.7±4.4 $$$
(kPa)	(2.21±0.72)	(4.58±0.93)	(2.87±0.80)	(4.08±0.59)
MPPL, mmHg	1.1±1.1	1.6±1.2 $$$	6.5±1.5 ***	7.0±1.2 ***
(kPa)	(0.15±0.15)	(0.21±0.16)	(0.86±0.20)	(0.93±0.16)
MLAP, mmHg	4.6±1.4	10.3±1.0 $$$	8.4±1.8 ***	12.0±1.0 $$$ ***
(kPa)	(0.61±0.19)	(1.37±0.13)	(1.12±0.24)	(1.60±0.13)
MRAP, mmHg	2.1±1.2	6.7±1.4 $$$	6.0±1.2 ***	9.1±0.8 $$$ ***
(kPa)	(0.28±0.16)	0.89±0.19)	(0.80±0.16)	(1.21±0.11)
MLAPtm, mmHg	3.5±1.2	8.6±1.2 $$$	1.9±1.8 *	5.1±0.9 $$$ ***
(kPa)	(0.47±0.16)	(1.14±0.16)	(0.25±0.24)	(0.69±0.12)
MRAPtm, mmHg (kPa)	1.0±1.3 (0.13±0.17)	5.0±1.2 $$$ (0.67±0.16)	-0.5±1.7 ** (-0.07±0.23)	2.2±1.3 $$$ *** (0.29±0.17)
CO, l/min	2.44±0.60	3.55±0.68 $$$	1.74±0.54 ***	2.59±0.50 $$$ ***
SV, ml/beat	16.6±3.7	30.7±6.8 $$$	10.3±3.2 ***	19.7±3.3 $$$ ***
PVR, 10^6*N*s*m^{-5}	39.3±15.2	55.5±20.8 $	62.6±22.4 *	58.4±12.1

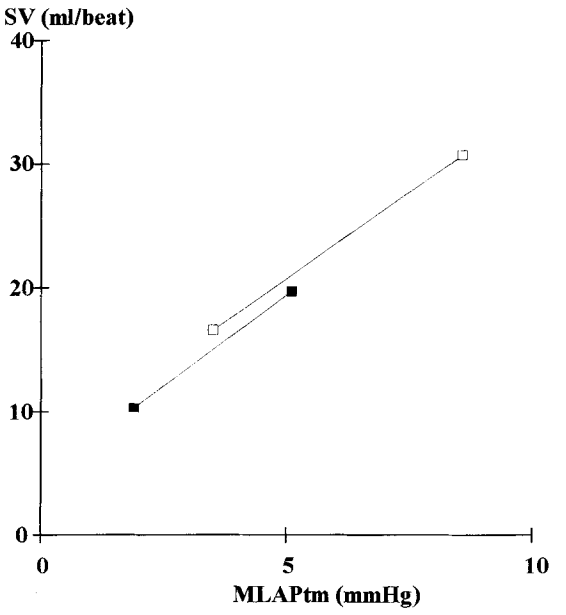

Figure 1. The pressure volume plots for the left side of the heart during IPPV (—□—) and CPPV (—■—) before and after volume loading.

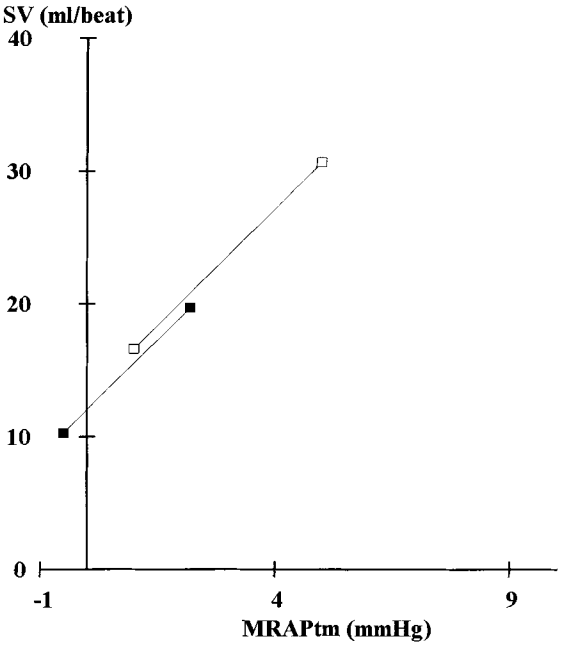

Figure 2. The pressure volume plots for the right side of the heart during IPPV (—□—) and CPPV (—■—) before and after volume loading.

Instead, the mechanisms behind the changes in SV should be sought primarily among the classical determinants of preload, contractility and afterload. An additional factor of interest is ventricular compliance. Considering that this study included the use of PEEP, motion abnormalities like an interventricular septal shift should also be mentioned (14).

Our study focused on the assessment of ventricular contractility. Usually this is defined in terms of force and velocity. We used an alternative method based on the change in SV to increasing preload, allowing for the construction of ventricular function curves. Essentially such function curves demonstrate Starling's law of the heart but a change in the slope also serves to indicate a change in contractility, provided that the other factors remain unaltered or otherwise under control.

The SV was determined by a conventional indicator dilution technique, while preload was estimated from the transmural mean atrial pressure. An important factor then is the adequacy of the technique by which the extramural pressure is measured. We utilized a balloon-tipped catheter where special attention was paid on keeping the filling volume constant. The balloon was positioned in the pleural space which we have earlier shown to compare favourably with the juxtacardiac position in the pericardial sac (Fig.3, (10)). It could be mentioned that this experiment was made with the similar thoracic drain in place as in the present study.

It should also be noted that utilizing variations in the transmural mean atrial pressure as an estimate of variations in preload presumes that this pressure reflects the ventricular end-diastolic volume and hence the end-diastolic fiber length. Obviously, concomitant changes in the ventricular wall compliance may obscure the validity.

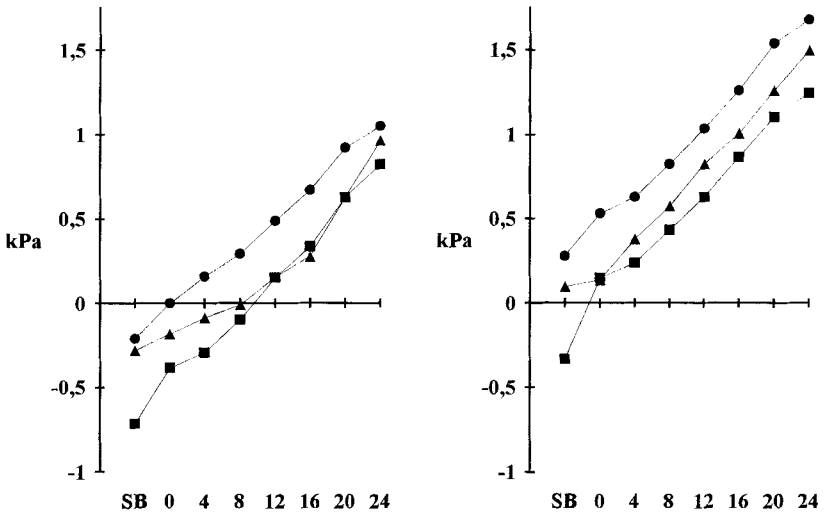

Figure 3. *The results of the simultaneous measures of the pressure sourounding the heart with balloon catheters placed in the pericardium (—▲—), oesofagus (—●—) and the pleural space (—■—). The balloons were filled with 0.2 ml (left) and 2.0 ml (right) of air. SB = spontaneous breathing. 0, 4, 8, etc. indicates the PEEP-level on cm H_2O. (From Haldén, Dissertation, 1980).*

As seen in Figs. 1 and 2, there were no differences between IPPV and CPPV in the inclinations of the ventricular function curves on either side of the heart. The apparent conclusion is that a PEEP of 15 cm H_2O did not affect myocardial contractility. This view is in agreement with a number of previous reports (12, 16, 17, 23, 24, 26) but is on the other hand in disagreement with others (13, 15, 19, 21) which invariably state that PEEP impairs contractility. Prewitt et al (20), however, infer that PEEP my actually enhance contractility.

Marini et al (17) used a model similar to ours. They speculated that the identical slopes do not exclude the possibility that a seemingly uninfluenced myocardial contractility during PEEP in fact might be the result of two opposing and neutralizing effects on the ventricular function, one enforcing and the other deteriorating. They mentioned two possibilities, either an increased compliance balanced by an impaired contractility or an improved contractility balanced by a decreased compliance.

Since there is no information that PEEP would induce increased ventricular compliance the second possibility appears less speculative. Disregarding the rather low probability that the effects would exactly balance each other, there is nevertheless a specific factor in the present study which might be argued to fit in with this latter alternative. When 500 ml of autologous blood was re-transfused, the SV increased by 14.1 ± 5.5 ml during IPPV and by 9.4 ± 2.5 ml during PEEP, a difference that might be seen to reflect a lower ventricular compliance during PEEP. There is, however, a more plausible explanation to this difference. Since the rise in intrathoracic pressure during PEEP causes an obstruction to venous return it is very likely that part of the transfused volume remains sequestered outside the thoracic cage, in essence, a diminution of preload.

As mentioned earlier, afterload may also influence SV. In the present study, it is the afterload on the right ventricle that is interesting. This factor is represented by the pulmonary vascular resistance, PVR. Before volume load, the application of PEEP induced a significant increase in PVR. After volume load there was no difference between the ventilation modes indicating that afterload was similar! This means that the post transfusion difference in SV between the ventilation modes could not have been caused by a difference in afterload. It is even unlikely that the pretransfusion difference in afterload was of any significance to the SV:s. A linear extrapolation of the right ventricular function curve during IPPV (Fig. 2) down to a point corresponding to the pretransfusion preload during PEEP reveals that the SV:s would have been the same inspite of any differences in afterload.

The increase in PVR when the shed blood was retransfused during IPPV probably demonstrates the pig's well known disposition to pulmonary vasoconstriction in response to a variety of stimuli (31). Apparently PEEP-ventilation attenuated this reaction by a mechanism which remains to be elucidated.

In summary, an overall evaluation of the results in the present study suggests that the differences in SV between the ventilation modes should not be ascribed to differences in contractility, but rather to the preload. The evaluation would, however, have gained further strength had the comparison been made under equal preload conditions.

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