Effects of Continuous Negative Extrathoracic Pressure Ventilation on Left Ventricular Dimensions and Hemodynamics in Dogs

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It has been reported that continuous negative extrathoracic pressure ventilation (CNETPV) depresses cardiac output less than continuous positive pressure ventilation (CPPV) does, and this difference may be related to the different effects of two ventilatory modes on preload. We performed simultaneous measurements of hemodynamics and left ventricular short axis dimensions by transesophageal echocardiography (TEE) to evaluate left ventricular preload and function during CNETPV and CPPV in normal dogs.

Hemodynamic measurements and simultaneous TEE recording were performed at 5 successive periods; 1) the first control period of intermittent positive pressure ventilation (IPPV1), 2) CNETPV with negative end-expiratory pressure (NEEP) of -10 cmH_2O (CNET10), 3) CNETPV with NEEP of -15 cmH_2O (CNET15), 4) the second control period of IPPV (IPPV2), and 5) CPPV with PEEP of 15 cmH_2O (CPPV15). Left ventricular end-systolic and end-diastolic dimension (LVESD and LVEDD), ejection fraction (EF) and fractional shortening (FS) were measured from TEE recordings.

Both CNET10 and CNET15 induced no significant changes in hemodynamics and left ventricular dimensions, compared with those during IPPV1. However, CPPV15 reduced cardiac output and stroke volume (SV) and increased heart rate significantly, compared with IPPV2. CPPV15 significantly decreased LVEDD compared with IPPV2. Neither EF nor FS showed any significant change throughout the experiment.

These results indicate that CNETPV preserved cardiac output because it maintained the preload and the left ventricular function. (Key words: negative pressure ventilation, hemodynamics, preload, transesophageal echocardiography)

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Continuous positive pressure ventilation (CPPV) improves oxygenation through augmentation of functional residual capacity (FRC)[1]. The same increment in FRC can be obtained by applying a constant external negative

pressure around the chest wall[2]. We have defined a ventilatory mode in which extrathoracic pressure is kept negative at end-expiration and further cyclic negative pressure induces tidal ventilation as continuous negative extrathoracic pressure ventilation (CNETPV)[3]. This mode of ventilation would offer the possibility of ventilating patients without the need for endotracheal intubation.

Skabulskis et al. reported that CNETPV produced the same improvement in oxygenation as CPPV did and CNETPV less depressed cardiac output than CPPV did in dogs with pulmonary edema[2]. We have also found that reduction in cardiac output during CNETPV was smaller than that during CPPV[4]. Additionally we found that central blood volume decreased during CPPV but did not change during CNETPV compared with intermittent positive pressure ventilation (IPPV)[5]. These differences in hemodynamics during CPPV and CNETPV may be related to differences in venous return. CNETPV may preserve or augment venous return due to reduced intrapleural pressure, while CPPV usually decreases venous return[6,7]. Transmural filling pressure has been used to evaluate preload, however, measuring transmural filling pressure seems to be inappropriate for assessing preload during CPPV and CNETPV, because precise measurement of juxtacardiac pressure is difficult in these conditions[8,9]. Therefore, evaluation of left ventricular end-diastolic volume is necessary to evaluate the changes in left ventricular preload during CNETPV and CPPV.

In human studies, it has been well known that left ventricular volume derived from echocardiographic measurement of short axis dimension correlates well with left ventricular volume determined by cineangiography[10]. The shape of a canine heart has been considered to be similar to that of a human heart[11]. Therefore, we measured left ventricular short axis dimensions by transesophageal echocardiography (TEE) to evaluate the changes in preload by CNETPV and CPPV in normal dogs.

Materials and Methods

Instrumentation

Eight mongrel dogs, weighing 8 to 14.5 kg, were anesthetized with 10 $mg \cdot kg^{-1}$ of ketamine (i.m.), followed by 50 mg of pentobarbital (i.v.). Intratracheal intubation was performed and mechanical ventilation was started with a Harvard constant-volume ventilator (OP-110, Okazaki Sangyo, Tokyo, Japan). The tidal volume was 15 $ml \cdot kg^{-1}$ with respiratory rate adjusted to maintain end-expiratory CO_2 tension around 40 mmHg and F_{IO_2} was 0.3. Anesthesia was maintained with halothane (0.3–0.5%) and fentanyl (20 $\mu g \cdot kg^{-1}$ bolus injection followed by continuous infusion at 5 $\mu g \cdot kg^{-1} \cdot hr^{-1}$). Muscle paralysis was obtained by pancuronium bromide. The animal received 5 $ml \cdot kg^{-1} \cdot hr^{-1}$ of lactated Ringer solution. Two flowo-directed thermodilution catheters (93A-431-H-7.5F, American Edwards, Santa Ana, CA) were inserted into the pulmonary artery and the right atrium. The catheter placed in the right atrium was used for injection of 5% dextrose of 0°C at the thermodilutional cardiac output measurement. Another catheter was inserted into the femoral artery for arterial blood pressure measurement and blood sampling.

CNETPV was performed as previously described[5]. The animal was placed in the cuirass which covered the animal from the neck to the upper abdomen. Then the dog and the cuirass were placed in a plastic bag which was sealed with a wide tape at the neck and the waist. Animals were

studied in the supine position. Negative body surface pressure to the chest and the upper abdomen was applied through a side port of the cuirass with KIMURA Negative Thoracic Pressure Ventilator (OKT-100, Kimura, Tokyo, Japan). Pressure around the chest wall was measured by a catheter fixed to another port of the cuirass.

Transesophageal echocardiography

A 5 MHz phased array transducer (PEF-511SA, Toshiba, Tokyo, Japan) was inserted into the esophagus and Toshiba SSH-160A Ultrasonograph was used for two dimensional echocardiographic imaging. The transducer was positioned to obtain a left ventricular short axis image at the chordae tendineae of the mitral valve. Echocardiographic images were recorded on a video tape for subsequent single frame stop-motion analysis. Left ventricular end-diastolic dimension (LVEDD) was measured at the frame that coincided with the peak of R wave of electrocardiograph, and end-systolic dimension (LVESD) was measured at the frame of the smallest ventricular cavity during a cardiac cycle. An average of three heart beats was used in all measurements.

Left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) were calculated from LVEDD and LVESD by the formulas described by Teichholtz[10]. Stroke volume (SV-TEE) was obtained from the difference between LVEDV and LVESV. Ejection fraction (EF) was obtained from calculation of SV/LVEDV. Fractional shortening (FS) was calculated as follows:

$$FS = (LVEDD\text{-}LVESD)/LVEDD$$

Protocol

Hemodynamic measurements and simultaneous TEE recording were performed at five successive periods; 1) the firrst control period of IPPV (IPPV1), 2) CNETPV with negative end-expiratory pressure of -10 cmH_2O (CNET10), 3) CNETPV with negative end-expiratory pressure of -15 cmH_2O (CNET15), 4) the second control period of IPPV (IPPV2), 5) CPPV with PEEP of 15 cmH_2O (CPPV15). Every measurement was performed at the end of the 20 min period of each ventilatory mode. During each measurement, the tidal ventilation was discontinued while PEEP or negative end-expiratory pressure (NEEP) were maintained. Hemodynamic measurements included mean arterial blood pressure (MAP), heart rate (HR), central venous pressure (CVP), and cardiac output determined by thermodilutional technique in triplicate. Stroke volume obtained from thermodilutional technique was referred as SV-THERMO. Systemic vascular resistance (SVR) were calculated by the standard formula.

Analysis

Results were expressed as the mean ± standard deviation. Statistical analysis was performed by the analysis of variance with repeated measures. When nonrandom variance was significant ($P < 0.05$), multiple comparison was made by using Bonferroni's modification of Student's t test. We compared IPPV1 with CNET10 and CNET15 and IPPV2 with CPPV15. We also compared IPPV1 with IPPV2 to evaluate time based changes in basal conditions.

In addition, in order to evaluate reliability of dimensional analysis of cardiac output by TEE, SV calculated by TEE (SV-TEE) was compared with that by thermodilutional technique (SV-THERMO) in 35 simultaneous measurements. Comparison between the percent changes in SV-TEE and SV-THERMO from the control value at IPPV1 was also performed

Table 1. All measured and derived variables of hemoddynamics and left ventricular dimensions during IPPV, CNETPV and CPPV

		IPPV1	CNET10	CNET15	IPPV2	CPPV15
HR	(beats·min^{-1})	101 ± 16	107 + 16	118 ± 22	91 ± 15	128 ± 11$
MAP	(mmHg)	91 ± 22	87 + 17	82 ± 18	87 ± 19	84 ± 21
CVP	(mmHg)	4.6 ± 3.0	3.4 ± 3.2	2.6 + 4.0	5.8 ± 2.8	9.8 ± 2.7$
cardiac output	(l·min^{-1})	1.5 + 0.6	1.7 ± 0.5	1.5 ± 0.4	1.5 ± 0.4	1.2 ± 0.3$
SV-THERMO	(ml)	16 ± 6.8	15.9 ± 4.8	13.3 ± 4.9	16.7 ± 4.8	9.4 ± 3.4$
SVR	(dyn·sec·cm^{-5})	5237 ± 2183	4269 ± 1302	4438 ± 1092	4564 + 1286	5215 ± 1753
LVEDD	(mm)	27.5 ± 4.2	26.9 ± 3.0	24.2 ± 3.4	28.2 ± 4.2	22.1 ± 4.0$
LVESD	(mm)	19.1 ± 3.0	19.4 ± 3.2	17.7 ± 2.4	21.3 ± 5.1	18.3 ± 4.0
EF		0.59 ± 0.1	0.57 + 0.08	0.55 ± 0.08	0.5 ± 0.2	0.39 ± 0.09
FS		0.31 ± 0.07	0.29 + 0.05	0.27 ± 0.05	0.26 ± 0.12	0.18 ± 0.04

Values are mean ± SD.
IPPV1 : initial control period of IPPV
CNET10 : CNETPV with negatie end-expiratory pressure of 10 cmH_2O
CNET15 : CNETPV with negative end-expiratory pressure of 15 cmH_2O
IPPV2 : second control period of IPPV
CPPV15 : CPPV with PEEP of 15 cmH_2O
HR : heart rate
MAP : mean arterial blood pressure
CVP : central venous pressure
SV-THERMO : stroke volume derived from thermodilution method
SVR : systemic vascular resistance
LVEDD : left ventricular end-diastolic dimension
LVESD : left ventricular end-systolic dimension
EF : ejection fraction
FS : fractional shortening
$: different from IPPV2, $P < 0.05$

using linear regression analysis.

Results

All measured and derived variabales are summarized in table 1.

Hemodynamics

Heart rate remained unchanged during CNETPV, and significantly increased during CPPV15 compared with that during IPPV2. Although CVP showed a tendency to decrease during CNETPV, these changes did not reach statistical significance. CPPV15 significantly increased CVP. MAP and SVR showed no significant change throughout the experiment. Cardiac output and SV-THERMO did not change during CNETPV, significantly compared with IPPV1. CPPV15 decreased cardiac output and SV-THERMO, compared with those during IPPV2.

Left ventricular dimensions

Both CNET10 and CNET15 induced no significant changes in LVEDD. However, CPPV15 produced a significant reduction in LVEDD. As LVESD showed a large variation among subjects during IPPV2 and CPPV15, there were no significant changes in LVESD. Neither EF nor FS showed any significant change throughout the experiment. Comparison between IPPV1 and IPPV2 revealed no significant difference in hemodynamics and left ventricular dimensions.

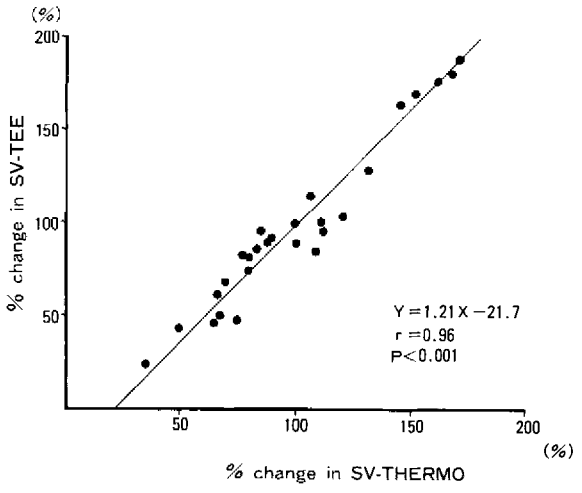

Fig. 1. Correlation between percent changes from the initial control value in SV-THERMO and those in SV-TEE.

SV-THERMO: stroke volume derived from thermodilution technique.

SV-TEE: stroke volume derived from left ventricular dimensions by transesophageal echocardiography.

Although comparisn of SV-TEE with SV-THERMO yielded a correlation coefficient of 0.76 ($P < 0.01$), there were considerable differences between SV-TEE and SV-THERMO in some subjects. A closer correlation was noticed between the percent changes from the initial control value in SV-TEE and those in SV-THERMO (fig. 1). By linear regression analysis, the relationship between these percent changes was found to be:

%(SV-TEE)=1.21*%(SV-THERMO) −21.7 (r=0.96, $P < 0.001$).

%(SV-TEE):
percent change in SV-TEE

%(SV-THERMO):
percent change in SV-THERMO

Discussion

The findings of this study are that CNETPV with NEEP of −10 cmH_2O and −15 cmH_2O induced no statistically significant changes in hemodynamics and left ventricular dimensions, whereas CPPV with PEEP of 15 cmH_2O decreased cardiac output, SV and LVEDD. Skabulskis et al. compared hemodynamic effects of CPPV with CNETPV under the conditions in which the levels of NEEP were adjusted to produce the same increment of FRC as CPPV did[12]. They reported that the absolute amount of NEEP which induced the equivalent increase in FRC was similar to a given level of PEEP, and that some animals needed slightly more transthoracic distending pressure during CNETPV. In our previous study, NEEP of −11.6 ± 1.8 cmH_2O (mean ± SD) produced the same increments in FRC as PEEP of 9.5 ± 1.5 cmH_2O, and the absolute values of NEEP were not statistically different from the levels of PEEP[5]. Therefore, FRC during CNET15 might be similar to that during CPPV15 in our study, but we did not measure the changes in FRC in the present study. We can not compare CNET15 with CPPV15 directly, since lung volumes in CNET15 and CPPV15 were not adjusted to be equivalent. Thus, we compared CNETPV or CPPV15 with the preceding control period of IPPV, and studied the difference in trends of hemodynamic changes caused by CNETPV and CPPV. We did not randomize the sequence of the ventilatory modes. Since no hemodynamic deterioration was noticed between IPPV1 and IPPV2, this probably did not affect the results.

Left ventricular dimensional analysis by echocardiography has been reported to be a reliable method for assessing left ventricular preload in humans[10]. Terai et al. reported that SV derived from left ventricular short axis dimension correlated well with SV derived from thermodilutional cardiac output measurement in patients mechanically ventilated with PEEP[13]. It has been known that the shape of canine left ventricle is similar to that of human ventricle[11]. Therefore, we measured left ventricular short axis dimensions to evaluate left ventricular volume. The results in this study demonstrated that correlation between absolute value of SV-TEE and SV-THERMO was fair, and that the percent changes from initial control value in SV-TEE correlated well with those in SV-THERMO. These results allow us to estimate relative changes in left ventricular volume by measuring changes in short axis dimensions in dogs.

It has been widely known that CPPV decreases cardiac output. The main reason for this phenomenon is generally believed to be reduction in venous return[7,8]. But some investigators reported that reduction in cardiac output was accompanied by rises in transmural right and left atrial pressure measured relative to intrapleural or esophageal pressure, and they argued that depressed left ventricular function should be one of the causes of reduced cardiac output[14,15]. Thus, the primary mechanism responsible for the decreased cardiac output during CPPV has been still controversial. The investigations, which studied left ventricular volume by echocardiography in humans[13] and by thermodilution technique in dogs[16], revealed that CPPV decreased the end-diastolic left ventricular volume. They also demonstrated that transmural filling pressure increased or stayed unchanged during CPPV despite reduction in left ventricular volume. This discrepancy between the pressure and the volume may have been due to errors in determination of the transmural pressure or altered ventricular compliance. Since CPPV and CNETPV induce considerable changes in intrathoracic pressure, determination of transmural pressure required precise measurement of juxtacardiac pressure. However, precise measurement of juxtacardiac pressure seems to be difficult, because of uneven distribution of pericardial pressure and changes in heart position induced by CPPV[8,9]. Moreover, it has been suggested that leftward displacement of interventricular septum induced by PEEP can restrict left ventricular filling and decrease left ventricular compliance[17]. In such conditions, filling pressure would not reflect changes in end-diastolic ventricular volume. Therefore, assessing left ventricular preload with transmural filling pressure seems to be inappropriate, and evaluation of left ventricular volume is necessary for studying preload. Results of this study indicate that CPPV decreased but CNETPV preserved the end-diastolic left ventricular volume estimated by LVEDD in normal dogs.

As CNETPV selectively decreases intrathoracic pressure, the gradient for venous return may increase. However, venous return may remain unchanged because some extrathoracic veins may collapse with extreme reduction in intrathoracic pressure[18]. The previous studies demonstrated that during CNETPV transmural right atrial pressure and transmural pulmonary capillary wedge pressure increased in dogs with oleic acid induced pulmonary edema but did not change in normal dogs[2,4]. In this study, left ventricular preload estimated by LVEDD did not change significantly during CNETPV. However, these results conflict with the previous report studying influ-

ences of Mueller maneuver on left ventricular volumes in humans, which indicated that large negative pleural pressure induced by Mueller maneuver increased left ventricular end-diastolic and end-systolic volume[18]. Mueller maneuver was performed from high lung volume or from FRC, and decreased pleural pressure to −30 mmHg. Both procedures increased left ventricular volume estimated by radionuclide angiography. But negative pleural pressure was maintained only for 20–25 seconds in those experiments. Therefore, the differences in species or the degree and duration of negative intrathoracic pressure may account for the differences in the results.

It has been pointed out that reduction in intrathoracic pressure during CNETPV might increase left ventricular afterload[2,18,19]. Left ventricular stroke volume frequently increases during inspiration under CPPV, because the increase in intrathoracic pressure could decrease transmural aortic pressure and reduce the impedance for left ventricular ejection from intrathoracic to extrathoracic compartments[19]. On the contrary, extreme reduction in intrathoracic pressure may increase the impedance for left ventricular outflow[18]. In fact, there was no significant increase in SVR in the previous and present studies[2,4]. Left ventricular end-systolic volume estimated by LVESD also did not change significantly. Therefore, the increase in afterload was not apparent in this level of NEEP. Further reduction in intrathoracic pressure would be required to affect afterload.

CNETPV induced on significant change in both ejection fraction and fractional shortening in this study. These parameters are useful indicators for evaluating left ventricular contractility when afterload and preload are maintained constant[20]. Since CNETPV did not seem to alter these conditions significantly, unchanged EF and FS observed in this study indicated that CNETPV maintained contractility of the left ventricle.

CNETPV with NEEP of −10 to −20 cmH_2O was shown to produce no hemodynamic deterioration in dogs with mild heart failure induced by fluid overload and pharmacological depression of contractility[12]. In that model, the increase in preload and afterload was expected to induce detrimental hemodynamic effects. Therefore, CNETPV seems to have minimal effects on preload and afterload in dogs with heart failure as well as in normal dogs. Hemodynamic stability would be one of the advantages of CNETPV as an alternative mode to CPPV. However, hemodynamic effects of CNETPV in critically ill patients could be different from those in canine models, because compliance characteristics of the chest wall and lungs of dogs are different from those of humans. Human studies will be necessary to define hemodynamic effects in patients who need intensive cares.

In conclusion, simultaneous measurements of left ventricular dimensions and hemodynamics demonstrated that CNETPV with NEEP of −10 cmH_2O and −15 cmH_2O induced no significant changes in left ventricular volumes and left ventricular function. These results suggest that CNETPV preserves cardiac output by maintaining preload and left ventricular function.

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