Baroreceptor-mediated compensation for hemodynamic effects of positive end-expiratory pressure

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Blevins, Stephen S., Martha J. Connolly, and Drew E. Carlson. Baroreceptor-mediated compensation for hemodynamic effects of positive end-expiratory pressure. J. Appl. Physiol. 86(1): 285–293, 1999.—The roles of the carotid arterial baroreceptor reflex and of vagally mediated mechanisms during positive end-expiratory pressure (PEEP) were determined in pentobarbital-anesthetized dogs with isolated carotid sinuses. Spontaneously breathing dogs were placed on PEEP (5–10 cmH2O) with the carotid sinus pressure set to the systemic arterial pressure (with feedback) or to a constant pressure (no feedback). Right atrial volume was measured with a conductance catheter. With carotid baroreceptor feedback before bilateral cervical vagotomy, total peripheral resistance increased (P < 0.01) and mean arterial pressure decreased (9.8 ± 4.3 mmHg) in response to PEEP. With no feedback after vagotomy, mean arterial pressure decreased to a greater extent (45 ± 6 mmHg, P < 0.01), and total peripheral resistance decreased (P < 0.05) in response to PEEP. In contrast, cardiac index decreased similarly during PEEP (P < 0.01) for all baroreceptor and vagal inputs. This response comprised a decrease in the passive phase of right ventricular filling (P < 0.01) that was not matched by the estimated increase in active right atrial output. Although the carotid baroreceptor reflex and vagally mediated mechanisms elicit vasoconstriction to compensate for the effects of PEEP on the arterial pressure, these processes fail to defend cardiac output because of the profound effect of PEEP on the passive filling of the right ventricle.

cardot arterial stretch receptor; cardiac output; conductance catheter; right atrial volume; total peripheral resistance; vagotomy

In the present study, we determined the effect of PEEP on several hemodynamic variables in the presence and absence of input from the carotid arterial baroreceptors and the vagal nerves. The results indicate that, during PEEP, baroreceptor and cardiopulmonary reflexes cause an increase in the active output of the right atrium and an increase in total peripheral resistance (TPR) to defend arterial pressure. However, these reflexes provide little or no defense of the cardiac output during PEEP because they fail to preserve the passive filling of the right ventricle during atrial diastole.

METHODS

Surgical preparation. Ten male mongrel dogs (20–22 kg in wt) were anesthetized initially with thiobalyl sodium (30 mg/kg), intubated, and then maintained at a surgical plane with halothane (2%). By using a sterile technique, an aortic flow transducer (16 mm, Transonic, Ithaca, NY) was placed through a midline thoracotomy. Then a conductance catheter was advanced through a purse string in the apex of the right atrial appendage so that the tip of catheter was located at the junction of the inferior vena cava and the right atrium, as has been described previously (6, 7). The leads from the flow probe and the conductance catheter were led through stab wounds in the thoracic wall and tunneled under the skin to exit near the base of the neck. The chest was then closed, and the residual air was evacuated. To minimize the changes in the electrical conductance of the blood due to splenic contraction during carotid hypotension (4), the dogs were splenectomized through a midline abdominal incision.

Five to seven days later, each dog was anesthetized with pentobarbital sodium (30 mg/kg) and intubated with a high-low jet endotracheal tube (NCC division, Mallinckrodt, Argyle, NY). Supplemental anesthetic was given as needed to prevent withdrawal reflexes, with the maintenance of the end-tidal CO2 between 4 and 5%. A catheter was placed in a femoral artery, advanced into the thoracic aorta, and connected to a pressure transducer (Statham P23AA) for the measurement of arterial pressure. A Swan-Ganz catheter was placed via a femoral vein to measure central venous pressure (CVP) and to calibrate the aortic flow measurements. A strain-gauge tip catheter (Millar Instruments, Houston, TX) was advanced from the remaining femoral vein into the right atrium at its junction with the inferior vena cava to measure dynamic atrial pressure.

Carotid sinus preparation. Left and right carotid sinus baroreceptors were perfused together and maintained at a constant pressure by using a blind sac preparation as described in detail previously (3). All small arteries in the area of each carotid sinus were ligated. Both lingual arteries were cannulated and connected to a common catheter for the measurement of carotid sinus pressure. The common carotid arteries were cannulated proximal to the carotid sinus and connected to a servo-controlled syringe pump that controlled

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carotid sinus pressure at any desired value. The aortic depressor nerves were left intact until the cervical vagi were severed completely later in the protocol.

Protocol. After surgical isolation of the carotid sinus region, the dog was allowed at least 60 min to stabilize with the carotid sinuses exposed to the dog’s systemic arterial pressure. The carotid sinuses were then exposed to each of four signals in random order: 1) systemic arterial pressure (closed loop); i.e. the natural feedback signal to the carotid arterial baroreceptors is present; 2) a constant pressure that would provide enough stretch of the carotid arteries to maintain the systemic arterial pressure near its value when the feedback loop is closed; 3) a pressure of 50 mmHg; and 4) a pressure of 200 mmHg. After 5 min of each condition of carotid sinus pressure, hemodynamic measurements were obtained during spontaneous respiration, then during mechanical ventilation with intermittent positive pressure during inspiration (IPPV), then during mechanical ventilation with PEEP, and finally during recovery from PEEP after removal from the ventilator. The hemodynamic measurements were made ~2 min after the onset of each state of ventilation and were complete by 5 min. Eight-second records of atrial conductance volume, CVP, and of atrial and systemic arterial pressure were acquired with a personal computer (486–66 MHz) at a rate of 200 samples/s by using the ASYST software package (Asyst Software Technologies, Rochester, NY). Aortic flow and carotid sinus pressure were monitored with a polygraph (Gould, Cleveland, OH). After the effect of positive-pressure ventilation was measured during each condition of carotid sinus input, the cervical vagi were ligated and transected bilaterally. The complete experimental sequence was then repeated after the dogs stabilized for at least 30 min with the carotid sinuses exposed to the systemic arterial pressure without mechanical ventilation. The sequence of signals presented to the carotid sinus baroreceptors was again randomized among dogs, except that carotid sinus pressure was always increased to 200 mmHg on the last trial. After vagotomy, this large increase in carotid sinus pressure was found in preliminary experiments to suppress the cardiac output greatly, especially during the application of PEEP. Because the recovery from this strong suppression was often slow and incomplete in the time frame of this protocol, this particular manipulation was not done until the end of the experiment. The magnitude of PEEP was 5 cmmH2O in the first five experiments and 10 cmmH2O in the last five experiments. Although the effect of PEEP on the measured variables tended to be greatest for 10 cmmH2O, there was no statistical difference for the two magnitudes of PEEP. Thus the means from all of the experiments were analyzed together and are presented in RESULTS.

Data analysis. TPR was determined as the difference between the mean arterial pressure (MAP) and CVP divided by the cardiac index. A computer algorithm (4) identified the onset of each right atrial contraction from the signals obtained with the conductance and strain-gauge tip catheters. The peak rate of increase in atrial pressure associated with the “a wave” in atrial pressure occurred ~30 ms before the peak rate of decrease in the atrial conductance signal. Accordingly, the algorithm was programmed to identify local maxima in the time derivative of the dynamic atrial pressure signal that occurred 30 ms before rapid decreases in atrial conductance volume. The rate of these decreases was required to exceed a criterion that was set on the basis of the overall strength and magnitude of the observed atrial contractions. The criterion was chosen to provide sufficient sensitivity to identify the atrial contractions without “false alarms.”

Mean values of the observed variables were tested statistically by using ANOVA corrected for repeated measures with respect to carotid sinus pressure and for repeated measures in the same dogs before and after vagotomy (23). When there was a significant overall effect by ANOVA, the differences among individual means were tested by computing the F-value for each simple main effect and then by the Newman-Keuls procedure as appropriate.

RESULTS

MAP responded significantly to the changes in carotid sinus pressure, as shown in Fig. 1. During spontaneous breathing before vagotomy, MAP decreased from 142 ± 6 to 70 ± 7 mmHg as carotid sinus pressure was increased from 50 to 200 mmHg (P < 0.01, Fig. 1A). After vagotomy this range of response increased significantly. When carotid sinus pressure was 50 mmHg, MAP was 175 ± 11 mmHg and greater than it was before vagotomy (P < 0.05). MAP was 65 ± 8 mmHg at the highest carotid sinus pressure. When carotid sinus pressure was fixed at 119 ± 5 mmHg before vagotomy or at 122 ± 6 mmHg after vagotomy to open the carotid baroreceptor feedback loop, MAP did not differ significantly from its closed-loop value when the carotid sinuses were exposed to the systemic arterial pressure during spontaneous breathing. Before vagotomy MAP did not respond significantly to mechanical ventilation.

![Fig. 1. Mean arterial pressure (MAP) before (A) and after (B) bilateral cervical vagotomy during spontaneous breathing (Spont), mechanical ventilation with intermittent positive pressure to drive inspiration (IPPV), IPPV with addition of positive end-expiratory pressure (PEEP), and after removal from ventilator (Recovery). Bilateral carotid sinus pressure (CSP) equals systemic arterial pressure to close feedback loop from carotid arterial baroreceptors (closed loop) or CSP is fixed at values (mmHg) shown. Values are means ± SE. Significantly different from value during Spont at same CSP: *P < 0.05; #P < 0.01. Significant difference for each state of ventilation: †from all other values, P < 0.05; ‡from CSP = 50 or 200 mmHg, P < 0.01.](http://jap.physiology.org/ Downloaded from)
with IPPV under any of the carotid sinus inputs (Fig. 1A). After vagotomy, MAP decreased in response to IPPV when the carotid sinus pressure was fixed at either 50 or 122 ± 6 mmHg (P < 0.01, Fig. 1B). MAP decreased significantly from its value during spontaneous breathing in response to PEEP in all cases (P < 0.01). Figure 2 shows the effect of vagotomy and removal of feedback from the carotid receptors on the responses of MAP for the cases where MAP during spontaneous breathing was not different from the closed-loop value. Note that the reduction in MAP by PEEP is greatest after vagotomy when the carotid sinus pressure is fixed to open the feedback loop and least when the loop is closed and the vagal input is intact.

Mean CVP did not respond significantly to the changes in carotid sinus pressure either before or after vagotomy. During spontaneous breathing at all values of carotid sinus pressure, CVP was −0.70 ± 0.24 mmHg before vagotomy and −1.26 ± 0.30 mmHg after vagotomy. These values did not differ significantly. CVP increased in response to IPPV (P < 0.01) by 0.95 ± 0.11 mmHg before vagotomy and by 1.66 ± 0.20 mmHg after vagotomy. CVP then increased further during PEEP compared with spontaneous breathing by 2.88 ± 0.42 mmHg before vagotomy and by 3.72 ± 0.29 mmHg after vagotomy. The increases in CVP during both IPPV and PEEP were greater after than before vagotomy (P < 0.05). However, the absolute values of CVP before and after vagotomy did not differ significantly during any state of ventilation. After the removal of PEEP, CVP returned to values not different from those observed initially during spontaneous breathing.

TPR responded significantly to the changes in carotid sinus pressure, as shown in Fig. 3. During spontaneous breathing before vagotomy, TPR decreased significantly as carotid sinus pressure was increased from 50 to 200 mmHg (P < 0.01, Fig. 3A). After vagotomy, TPR also decreased significantly as carotid sinus pressure was increased (P < 0.01, Fig. 3B). During spontaneous breathing under all conditions except when the carotid feedback loop was closed, TPR was greater after vagotomy than it was before vagotomy (P < 0.05 in each case). Before vagotomy, TPR increased significantly in response to mechanical ventilation with IPPV when the carotid sinus pressure was set to 200 mmHg (P < 0.01, Fig. 3A). During the application of PEEP, TPR was significantly greater than it was during spontaneous breathing when the carotid feedback loop was closed and when the carotid sinus pressure was set at 200 mmHg (P < 0.01, in each case). After vagotomy, TPR did not change significantly in response to IPPV or PEEP except when the carotid sinus pressure was fixed at 122 ± 6 mmHg (Fig. 3B). Under this open-loop condition, TPR was significantly less during IPPV and PEEP than it was during spontaneous breathing (P < 0.05, in each case). Figure 4 shows the effect of vagotomy and removal of the feedback from the carotid receptors on the responses of TPR for the cases where the MAP during spontaneous breathing was not different from the closed-loop value. Note that the increase in TPR during PEEP is greatest when both the carotid feedback loop is closed and the vagi are intact. When the feedback loop is opened after vagotomy, TPR decreases in response to PEEP.

Heart rate responded significantly to the changes in carotid sinus pressure, as shown in Fig. 5. During spontaneous breathing before vagotomy, heart rate decreased significantly as carotid sinus pressure was increased from low and intermediate values to 200 mmHg (P < 0.01, Fig. 5A). After vagotomy, heart rate decreased progressively and significantly as carotid sinus pressure was increased from 50 mmHg (P < 0.01, Fig. 5B). Before vagotomy, heart rate increased significantly in response to mechanical ventilation with IPPV and with PEEP at all values of carotid sinus pressure (P < 0.01 in each case, Fig. 5A). After vagotomy, heart rate also changed significantly in response to IPPV (P < 0.05) or PEEP (P < 0.01) except when the carotid sinus pressure was set to 200 mmHg (Fig. 5B). Heart rate also increased significantly in response to mechanical ventilation with IPPV and with PEEP at all values of carotid sinus pressure (P < 0.01 in each case, Fig. 5A). After vagotomy, heart rate also changed significantly in response to IPPV (P < 0.05) or PEEP (P < 0.01) except when the carotid sinus pressure was set to 200 mmHg (Fig. 5B). Heart rate also increased significantly in response to mechanical ventilation with IPPV and with PEEP at all values of carotid sinus pressure (P < 0.01 in each case, Fig. 5A). After vagotomy, heart rate also changed significantly in response to IPPV (P < 0.05) or PEEP (P < 0.01) except when the carotid sinus pressure was set to 200 mmHg (Fig. 5B). Heart rate also increased significantly in response to mechanical ventilation with IPPV and with PEEP at all values of carotid sinus pressure (P < 0.01 in each case, Fig. 5A). After vagotomy, heart rate also changed significantly in response to IPPV (P < 0.05) or PEEP (P < 0.01) except when the carotid sinus pressure was set to 200 mmHg (Fig. 5B).
spontaneous breathing before vagotomy, cardiac index decreased significantly as carotid sinus pressure was increased from low and intermediate values to 200 mmHg (\(P<0.01\), Fig. 7A). After vagotomy, cardiac index also decreased significantly in response to PEEP at all values of carotid sinus pressure (\(P<0.01\) in each case, Fig. 7B). Figure 8 shows the effect of vagotomy and removal of feedback from the carotid receptors on the responses of cardiac index for the cases where the MAP during spontaneous breathing was not different from the closed-loop value. Note that the significant decreases in cardiac index during PEEP do not differ statistically whether the carotid feedback loop is closed or open or whether the vagi are intact.

Changes in right atrial volume were estimated with the conductance catheter in seven dogs before vagotomy and then again after vagotomy in six of these seven dogs. Although atrial stroke volume and stroke work responded to large changes in carotid sinus pressure as was reported previously (4), these variables did not change significantly with the application of either IPPV or PEEP at any setting of carotid sinus pressure.

Active atrial output was calculated as the product of heart rate and atrial stroke volume to estimate the active filling of the right ventricle during the atrial contraction. This variable was then subtracted from the aortic flow to estimate the passive ventricular filling that occurred during the relaxation of the atrium. Figure 9 shows the effect of vagotomy and removal of feedback from the carotid receptors on the responses of both the active and passive right ventricular filling for the cases where the MAP during spontaneous breathing was not different from the values when the carotid feedback loop was closed. When the carotid sinuses were exposed to the systemic arterial pressure before vagotomy, the application of IPPV elicited an increase in the atrial output (\(P<0.01\)) that was sustained with further application of PEEP (Fig. 9, top). This response reversed with the return to spontaneous breathing. After vagotomy, atrial output did not increase significantly in response to either IPPV or to PEEP, whether the carotid feedback loop was opened or closed (Fig. 9, top). These responses after PEEP and vagotomy were significantly less than the corresponding responses with the vagi intact (\(P<0.05\)). Passive ventricular

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**Fig. 3.** Total peripheral resistance (TPR; in mmHg-min-kg/ml⁻¹) before (A) and after (B) bilateral cervical vagotomy during Spont, mechanical ventilation with IPPV, IPPV with addition of PEEP, and Rec. Bilateral CSP equals systemic arterial pressure to close feedback loop from carotid arterial baroreceptors (closed loop), or CSP is fixed at values (mmHg) shown. Values are means ± SE. Significantly different from value during Spont at same CSP: *\(P<0.05\), #\(P<0.01\). Significant difference for each state of ventilation: \(^a\)from all other values, \(P<0.05\); \(^b\)from CSP = 50 or 200 mmHg, \(P<0.05\); \(^c\)from value when CSP = 119 or 200 mmHg, \(P<0.05\).

**Fig. 4.** Changes in TPR in response to mechanical ventilation with IPPV, IPPV with addition of PEEP, and during Rec. Bilateral CSP equals systemic arterial pressure to close feedback loop from carotid arterial baroreceptors (closed loop), or CSP is fixed at intermediate values shown in Fig. 3 (open loop) in intact or VGX condition. Values are means ± SE. Significantly different from 0: *\(P<0.05\), #\(P<0.01\). Significant difference for each state of ventilation: \(^a\)from all other values, \(P<0.05\); \(^b\)from closed loop-intact or open loop-VGX, \(P<0.05\).
filling was depressed during positive pressure ventilation. IPPV led to a significant decrease in the filling that then decreased further with the application of PEEP (P < 0.01, in each case). This response reversed with the resumption of spontaneous breathing (P < 0.01, Fig. 9, bottom). Although the decreases in passive filling that occurred during IPPV or PEEP were greatest when the vagi were intact, the differences from the corresponding responses after vagotomy were not significant.

DISCUSSION

The application of PEEP has long been known to suppress cardiac output (22). This effect of PEEP has been attributed to a variety of factors but, at the level of PEEP used in the present study, the volume of both the left and right ventricles is reduced, as has been shown by echocardiography (1, 11), ultrasonic measurements of ventricular diameters (17), and magnetic resonance imaging (12). This reduction in volume appears to be secondary to decreased venous return that is caused by the increase in intrathoracic pressure during PEEP that compresses the heart (22) and the great veins (8). PEEP also evokes a heart-lung interaction (22) characterized by an increase in right ventricular afterload that may suppress right ventricular output and flatten the ventricular septum (11). PEEP has also been reported to suppress myocardial contractility by humoral (10, 14) or other mechanisms. However, clear evidence for a decrease in contractility has been lacking in many studies (22). Moreover, fluid infusion that increases venous return and atrial dimensions can reverse the decrease in cardiac output that occurs during PEEP (7, 16).

The present study was designed to test the ability of the carotid arterial baroreceptor reflex and of vagally mediated reflexes to offset the suppressive effects of PEEP on hemodynamics. The separate role of the aortic arch baroreceptors was not determined because we did not manipulate their input independently or determine the effects of selective ligation of the aortic depressor nerves. Rather, vagotomy in this experiment removed both afferent and efferent pathways to all of the vagally innervated structures below the neck. Our findings show that the effect of PEEP to reduce MAP is least when the afferent inputs from the carotid arterial baroreceptors and from the vagus nerves are present (Fig. 2). Thus we have clear evidence that the arterial baroreceptors help to maintain arterial pressure in the face of PEEP. Our data also indicate that the primary mechanism for this response is an increase in TPR (Fig.
4). The increase in resistance does not occur in the absence of input from the carotid arterial receptors and the vagi. In this latter case, PEEP elicits a decrease in resistance that is likely to be an autoregulatory response of the systemic vasculature that attempts to maintain blood flow in the face of the hypotension that results from PEEP.

Our data suggest that neither the reflex-mediated increases in cardiac contractility and heart rate (Fig. 6) nor the decreases in systemic vascular capacity (21) are sufficient to overcome the mechanical effects of PEEP that impede the venous return and cardiac output (Fig. 8). PEEP has been shown to cause an increase in hepatic blood volume (9, 18) that accompanies an increase in hepatic venous pressure and a decrease in hepatic blood flow (2). Thus the accumulation of blood within the liver appears to be a major component of the effect of PEEP on venous return. We suggest that this effect overwhelms any compensation by the baroreceptor reflexes that would serve to maintain the cardiac output. Splenic contraction during PEEP has been reported to compensate partially for the effects of PEEP on hepatic hemodynamics (18). However, this compensation was absent by design in the splenectomized dogs that we studied. This situation may have increased the effect of PEEP to reduce the cardiac output in our experiments.

A conductance catheter was used to estimate the changes in the volume of the right atrium, as has been described previously (4, 5). Although the signal from the catheter has been shown to be nearly linear with volume (4), the slope of the relationship of the measured volume to the true volume deviates from unity by as much as 29%. Even with this limitation, the measurements of atrial conductance volume in the present study (data not shown) and in an earlier report (5) estimate that an average of 20% of the ventricular filling occurs during the atrial contraction at heart rates below 140 beats/min, as was also found using cineangiography (15). Using the measurements of atrial volume and aortic flow, we estimated both the ventricular filling that occurred during the atrial contraction as well as the passive ventricular filling that occurred while the right atrium was relaxed. Our estimate of the active atrial output may exceed the actual contribution of the atrial contraction to the ventricular filling to the extent that there is reflux of blood into the vena cava during the atrial beat. However, at high heart rates of ~200 beats/min when the passive ventricular filling is small because of the short duration of the ventricular diastole, our previous work suggests that the amount of reflux is generally <20% of the active atrial output (5). Our present findings suggest that the active contribution of the right atrium actually increases in response to positive-pressure ventilation when the vagus nerves...
are intact and the carotid sinus pressure is in its midrange (Fig. 9). This increase is primarily the result of an increase in heart rate because the estimated increase in the right atrial stroke volume is not significant. The total right atrial volume was not determined in these experiments, but previous work (7) has shown that PEEP causes a decrease in the total atrial volume. The maintenance of the atrial stroke volume in the face of the decrease in total volume indicates that the contractility of the atrium increases with the application of PEEP. The increase in atrial output occurs whether the carotid sinus is exposed to the systemic arterial pressure or is held constant at an intermediate value. Thus the carotid baroreflex control of right atrial contractility that we reported previously (4) is not required for the estimated increase in active right atrial output. This response does require either afferent or efferent (13) vagal pathways because it is not present after vagotomy. The increases in heart rate in response to IPPV and PEEP are attenuated by vagotomy, so that the change in rate may not be sufficient to cause a significant change in the active output of the atrium. When carotid sinus pressure was fixed at either 50 or 200 mmHg, the active atrial output did not change significantly in response to positive-pressure ventilation (data not shown). At the low value of sinus pressure, it is possible that the atrial output was near maximal. The high value of pressure may have pro-

**Fig. 9.** Changes in active right ventricular filling that occurs during right atrial contraction (top) and in passive filling (cardiac index-active filling, bottom) in response to mechanical ventilation with IPPV, IPPV with addition of PEEP, and during recovery. Values are means ± SE. Bilateral CSP equals systemic arterial pressure to close feedback loop from carotid arterial baroreceptors (closed loop), or CSP is fixed at intermediate values shown in Fig. 7 (open loop) in intact or VGX condition. Significantly different from 0: *P < 0.05, #P < 0.01. *Significantly different from intact values for same state of ventilation, P < 0.05.

**Fig. 10.** MAP plotted as a function of bilateral CSP during Spont and mechanical ventilation with PEEP under conditions when CSP was fixed before (A) and after VGX (B).
vided enough inhibition on the autonomic control of the right atrium to prevent the response.

The estimated passive filling of the right ventricle that occurred during the right atrial diastole was affected strongly by the positive-pressure ventilation. With the application of IPPV, the decrease in this passive filling was similar in magnitude to the increase in right atrial output (Fig. 9). Thus the total filling of the ventricle and hence the cardiac index (Fig. 8) was maintained during IPPV. PEEP led to a further decrease in passive filling that was significant regardless of the state of the carotid baroreflex or of the vagi. In all cases the estimated active output of the atrium failed to compensate for this decrease in passive filling due to PEEP (Fig. 9), so that cardiac index decreased significantly (Fig. 8). These results indicate that, in the acutely prepared, anesthetized, but otherwise healthy splenectomized dog, autonomic reflexes alone cannot compensate for the reduced right ventricular filling that occurs in response to PEEP.

Our design differs from others that have addressed the interaction of the baroreceptor reflex with PEEP because these previous studies examined the effect of PEEP on the baroreceptor reflex, whereas the present study tested the ability of the reflex to compensate for the hemodynamic effects of PEEP. Figure 10 plots the relationship of the systemic arterial pressure to the carotid sinus pressure during spontaneous breathing and during PEEP. The plot suggests that the slope or open-loop gain of the baroreceptor reflex is similar in the presence or absence of PEEP, whereas the entire relationship is shifted downward. This result contrasts with that of Sepe et al. (19), who found a decrease in the gain of the reflex during PEEP in rabbits. It is possible that the addition of more points at intermediate values of carotid arterial pressure to our data would reveal a similar effect on the gain, but it is more likely that there is a species difference between dogs and rabbits. Sham et al. (20) varied the pattern of positive airway pressure in cats and found no effect of a change in pattern on the gain of the reflex. As the amount of PEEP was increased in their study, the gain of the reflex decreased slightly but not significantly both before and after vagotomy. This result is similar to our findings in Fig. 10.

In terms of reflex compensation for the effects of PEEP, our results suggest strongly that the compensation is not effective in opposing any of the decrease in cardiac output that occurs with PEEP. Because the infusion of volume can reverse the decrease in cardiac output during PEEP (7, 16), our results underscore the importance of maintaining the optimal blood volume for adequate tissue perfusion when PEEP is used therapeutically.

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