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Hemodynamic Benefit of Positive End-expiratory Pressure during Acute Descending Aortic Occlusion

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Background: **Acute aortic occlusion in vascular surgery patients abruptly increases arterial resistance and blood pressure, which, in turn, makes subsequent volume expansion during cross-clamp application difficult. The use of vasodilatory drugs or volatile anesthetic agents to attenuate this response may have persistent detrimental effects after clamp removal. Another potential therapy that produces rapid effects on myocardial loading conditions is positive end-expiratory pressure (PEEP). In a porcine model of acute aortic clamping, the hemodynamic consequences of 15 cm H_2O PEEP with and without plasma volume expansion were studied.**

Methods: **Forty anesthetized pigs underwent 30-min occlusion of the abdominal aorta 1 cm above the origin of the celiac artery. Animals were randomly divided into four treatment groups (n = 10 each) to receive 15 cm H_2O PEEP or zero end-expiratory pressure (ZEEP) with or without plasma volume expansion using 6% hetastarch (10 ml/kg) during cross-clamp application. Mean aortic pressure was measured with a transducer-tipped catheter placed in the ascending aorta; stroke volume was calculated using thermodilution cardiac output. End-expiratory pressure was discontinued upon aortic declamping, and animals were studied over the ensuing 30-min period.**

Results: **Aortic occlusion doubled systemic vascular resistance in all groups. Mean aortic blood pressure increased significantly in both ZEEP groups at 1 and 5 min but not in animals treated with 15 cm H_2O PEEP. The application of PEEP with aortic cross-clamping reduced cardiac output and stroke volume by nearly 50%. Cardiac output and stroke volume increased after volume expansion regardless of end-expiratory pressure. After aortic declamping, aortic blood pressure decreased in all groups but was significantly greater in the PEEP + volume group than in either ZEEP group. Similarly, 5 min after declamping, stroke volume was greatest in the PEEP + volume animals.**

Conclusions: **Fifteen cm H_2O PEEP reduces the hypertensive response to acute aortic occlusion and allows concomitant volume expansion. Consequently, stroke volume and blood pressure are better maintained after clamp removal in PEEP + volume animals. The use of PEEP during acute aortic occlusion in patients may allow rapid control of loading conditions to attenuate systemic hypertension while permitting simultaneous volume expansion.**

THE intraoperative treatment of patients undergoing major aortic surgery requiring cross-clamping of the thoracic or abdominal aorta can be difficult and challenging. Frequently, these patients have underlying hypertension[1] or coexisting coronary artery disease with variable amounts of left ventricular (LV) contractile dysfunction,[2,3] both of which can dramatically alter the hemodynamic response to acute aortic occlusion. Depending on the level of occlusion, aortic cross-clamp can abruptly increase LV afterload and preload,[4] and these stresses may place patients at particular risk for perioperative myocardial ischemia.[5]

Measures to reduce the hemodynamic responses to acute aortic occlusion include hemodilution and the careful titration of volatile anesthetic agents and vasodilators.[4,6] However, each of these maneuvers carries distinct disadvantages. For example, isovolemic hemodilution, while reducing the increment in systemic vascular resistance during occlusion, also produces greater hemodynamic instability and hypotension during reperfusion, requiring six times greater dosages of phenylephrine.[7] Volatile anesthetic agents cause direct myocardial depression that can attenuate the intrinsic contractile response to an abrupt increase in LV afterload and have tissue concentrations that preclude rapid removal after clamp release.[6] Vasodilators, such as nitroglycerin, may reduce the increment in preload and promote coronary subendocardial vasodilation but elicit a weak response relative to the large increase in vascular resistance.[8] More potent vasodilators, such as sodium nitroprusside, are effective to reduce aortic pressure but decrease splanchnic perfusion below the level of aortic occlusion with potential visceral injury.[9,10] Another complicating factor is that to attenuate declamp hypotension, volume expansion must be administered during aortic occlusion.[11–14] However, volume expansion during aortic occlusion may be difficult in the face of systemic hypertension imposed by the cross-clamp because of an increase in stroke volume and further hypertension. All of these factors occurring at varying magnitudes during aortic cross-clamping make tight control of aortic blood pressure difficult and unpredictable.

The use of positive end-expiratory pressure (PEEP) during cross-clamp application may represent a potentially attractive therapeutic consideration. PEEP is easily titrated and has a rapid onset with short-lived hemodynamic consequences after discontinuation. PEEP has known effects on transmural filling pressures with preload-reducing and afterload-reducing benefits.[15,16] We tested the hemodynamic benefit of 15 cm H_2O PEEP in a porcine model of supraceliac aortic cross-clamping with and without concomitant volume expansion followed by a period of aortic declamping.

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Materials and Methods

Animal Profiles and Surgical Specimens

Animals were handled according to the guidelines approved by the American Physiologic Society and the Guide for the Care and Use of Laboratory Animals, published by the National Institutes of Health (publication 85–23, revised 1996). The Institutional Animal Care and Use Committee of the University of Texas Medical Branch approved this study. Animals were allowed *ad libitum* water intake up to the time of surgery.

General anesthesia was induced using ketamine (20 mg/kg intramuscularly) in 40 mature, female Yorkshire pigs weighing 30.6 ± 2.9 kg (range, 25–36 kg). After tracheal intubation, each animal was ventilated with a tidal volume of 15 ml/kg using an air and oxygen mixture.

The respiratory rate was adjusted to maintain normocapnia as measured by capnography (Datex Instrumentation, Helsinki, Finland). Anesthesia was deepened with a bolus dose of fentanyl (15 μg/kg) and diazepam (0.2 mg/kg) followed by a continuous infusion of fentanyl (10 $\mu g \cdot kg^{-1} \cdot h^{-1}$) and diazepam (0.3 $mg \cdot kg^{-1} \cdot h^{-1}$) through a catheter inserted in a lateral auricular vein. During the surgical preparation, isoflurane (0.5–1.5% inspired concentration) was administered as necessary to maintain a sufficient depth of anesthesia using standard clinical criteria.[17] Muscle paralysis was provided by 0.1 mg/kg pancuronium administered intravenously as necessary to prevent shivering. In all animals, during aortic cross-clamping, isoflurane was maintained at 1.5% end-tidal concentration, which was then decreased to 0.5% end-tidal concentration immediately before and throughout declamping.

A 20-cm catheter was inserted into the femoral artery by cutdown and threaded intraabdominally into the common iliac artery. A thermodilution catheter was inserted through a side branch of the right internal jugular vein into the pulmonary artery. Core temperature was recorded using the thermistor on the pulmonary artery catheter.

Through a median sternotomy incision, fluid-filled catheters were inserted into the aorta *via* the right internal mammary artery and into the superior vena cava *via* the right internal mammary vein. A micromanometer-tipped catheter (MPC-500, Miller Instruments, Houston, TX) was inserted into the aorta *via* the left internal mammary artery and was recalibrated according to the fluid-filled catheter in similar location. Over the anterior free wall of the left ventricle, two 3-mm diameter holes were made in the pericardium, and a pair of ultrasonic dimension transducers was implanted into the LV subendocardium. The ultrasonic signals were received and analyzed instantaneously to measure LV dynamic distances (model 301 Sonmicrometer, Triton Technology, San Diego, CA). The median sternotomy incision was tightly reapproximated. Through a midabdominal incision, the descending aorta was isolated 1 cm above the origin of the celiac artery and loosely encircled with an umbilical tape snare. Heparin (300 U/kg) was administrated to prolong the activated clotting time (ACT) more than 250 s. Repeat ACT measurements were taken hourly, and additional doses of heparin (150 U/kg) were added as necessary.

Protocol

Animals were assigned using a random numbers table to one of four groups: zero end-expiratory pressure (ZEEP; n = 10); ZEEP + volume expansion (n = 10); 15 cm H_2O PEEP (n = 10); 15 cm H_2O PEEP + volume expansion (n = 10). PEEP therapy was initiated in appropriate animals throughout the aortic occlusion and was discontinued at the time of reperfusion. A basal infusion of 0.9% saline was administered in all animals at 5 $ml \cdot kg^{-1} \cdot h^{-1}$ during instrumentation and throughout the experimental protocol. In the animals receiving volume expansion, 6% hetastarch solution was administered intravenously at 10 ml/kg within the period of aortic occlusion. No additional fluid was administered during cross-clamp release.

After baseline measurements were recorded, the descending aorta was acutely occluded by tightening the tape through the rubber snare for 30 min. Repeat measurements, including proximal (internal mammary artery) and distal (femoral artery) aortic pressures, were recorded at 1, 5, and 30 min during aortic occlusion. Next, the occlusion was released, and measurements were acquired 1, 5, and 30 min during reperfusion. No vasoactive drugs or sodium bicarbonate were administered throughout the study. During aortic occlusion, the isoflurane concentration was maintained at 1.5% end-expiratory concentration, which was then reduced to 0.5% end-expiratory concentration immediately before and throughout reperfusion. At the conclusion of each experiment, the heart was arrested with a lethal injection of potassium chloride solution.

Measurements

Fluid-filled transducers were zeroed against atmospheric pressure at the anterior axillary level and calibrated with a mercury manometer. Hemodynamic variables recorded at end-expiration (Model ES-1000, Gould, Inc., Valley View, OH) included mean aortic pressure, mean pulmonary artery pressure, central venous pressure, pulmonary artery wedge pressure, and heart rate. Arterial blood gases (model 1306, Instrumentation Laboratory, Lexington, MA) and serum hemoglobin (Cooximeter model 482, Instrumentation Laboratory) were repeatedly measured throughout the experiment. Mean cardiac output was determined using thermodilution by averaging two 5-ml injections of iced saline solution injected at end-expiration. Stroke volume (ml/beat) was calculated as (mean cardiac output × 1,000)/

heart rate. LV end-diastolic segment length was measured under the QRS complex of the electrocardiogram immediately before the major aortic pressure inflection; LV end-systolic segment length was measured at the dicrotic notch of aortic pressure.[18] Segmental shortening (%) was calculated as ([end-diastolic length] − [end-systolic length]/end-diastolic length) × 100. Systemic vascular resistance (dyn · s · cm^{-5}) was calculated as ([mean aortic pressure − central venous pressure]/cardiac output) × 79.9. LV stroke work (g × m) was calculated as ([stroke volume] × [mean aortic pressure − pulmonary artery wedge pressure]) × 0.0136.

Statistical Analysis

Data, expressed as mean ± SD, were analyzed using analysis of variance for a three-factor factorial experiment with repeated measures. The three factors were PEEP (0 and 15 cm H_2O), volume expansion (6% hetastarch, 0 and 10 ml/kg), and time (five measurement intervals). Effects and interactions were assessed at significance level of 0.05. We adjusted for multiple comparisons using Fisher's least significant difference procedure with $P < 0.005$ for a comparison-wise error rate.

Results

The study was successfully completed in all animals. Acute aortic occlusion caused systemic vascular resistance to double in all groups (table 1). As seen in figure 1, after 1 and 5 min of aortic occlusion, mean aortic blood pressure significantly increased in both ZEEP groups but not in animals treated with 15 cm H_2O PEEP. Accordingly, mean aortic pressure was 25–35% lower with PEEP than ZEEP in respective groups. Cardiac output (table 1) and stroke volume (fig. 2) remained constant in both ZEEP groups. In contrast, the application of PEEP in combination with aortic cross-clamp reduced cardiac output and stroke volume by nearly 50%. Aortic cross-clamping caused a significant increase in LV stroke work in ZEEP animals, whereas PEEP reduced stroke work by 40% (table 1). Although LV segmental shortening remained unchanged with aortic occlusion, end-diastolic and end-systolic segment lengths increased in ZEEP animals, whereas PEEP attenuated this response. Filling pressures (central venous pressure and pulmonary artery wedge pressure) increased with aortic cross-clamp in all groups. Aortic pressures measured distal to the cross-clamp decreased similarly in all groups during aortic occlusion (table 1).

Volume expansion during cross-clamp application increased cardiac output in PEEP and ZEEP groups (table 1). Stroke volume and stroke work tended to decrease 30 min after cross-clamp without volume expansion, but each was maintained constant in animals receiving Hespan. Similarly, end-diastolic segment length decreased significantly in both groups without volume expansion while remaining unchanged in Hespan-treated animals. After 30 min of aortic cross-clamp, serum hemoglobin increased without volume expansion but decreased with volume expansion (table 2).

Acute aortic declamping markedly reduced systemic vascular resistance and filling pressures in all animals (table 1). Mean aortic blood pressure decreased significantly with clamp removal in all animals, with the largest decrease seen in both ZEEP groups irrespective of volume expansion (fig. 1). Cardiac output decreased in the ZEEP animals with or without volume expansion but increased significantly in both PEEP groups, particularly in animals receiving Hespan. Thirty minutes after cross-clamp removal, cardiac output remained greater in both volume-expanded groups and was not different from baseline values. Stroke volume and stroke work were significantly greater in the PEEP + volume group 5 min after declamping (fig. 2). Declamping caused serum hemoglobin to increase in all groups as end-diastolic segment length increased only after removal of 15 cm H_2O PEEP. Segmental shortening was significantly lower than baseline values in both ZEEP groups with or without volume expansion.

Oxygenation variables are shown in table 2. As expected, arterial pH decreased significantly but similarly in all groups with early reperfusion. Thirty minutes after cross-clamp removal, pH values remained lower than baseline in all groups. Although carbon dioxide tension increased with declamping, arterial bicarbonate concentrations decreased and remained lower than baseline throughout reperfusion. Base deficit values increased in all groups during declamping, with only partial recovery by the conclusion of the experiment without intergroup differences.

Discussion

In this porcine model, 15 cm H_2O PEEP reduces the hypertensive response to acute aortic occlusion and allows concomitant volume infusion, which, in turn, reduces the degree of declamp hypotension by improving stroke volume. This study confirms the independent benefit of volume expansion during cross-clamp application as indicated by a greater stroke volume after declamping; others have reported similar results.[11] However, PEEP alone produces a similar benefit on stroke volume during declamping as the ZEEP + volume animals demonstrated, indicating that PEEP, by attenuating venous return, may increase splanchnic venous capacitance during aortic cross-clamping. The clinical implication is that the use of PEEP during aortic occlusion in patients may allow rapid control of loading conditions to attenuate systemic hypertension while allowing simultaneous volume expansion. The discontinuation of PEEP with cross-clamp removal can lead to an improvement in stroke volume so that early declamp hypotension is attenuated.

Table 1. Hemodynamic Variables throughout the Experimental Procedure

Variable	Group	Baseline	Aortic Clamp			Aortic Declamp		
			1 min	5 min	30 min	1 min	5 min	30 min
Heart rate (beats/min)	ZEEP	96 ± 25	87 ± 29	95 ± 18*	162 ± 18*	149 ± 20	128 ± 21*	114 ± 20*†
	ZEEP + volume	97 ± 22	89 ± 15	103 ± 21*	162 ± 18*	157 ± 22	140 ± 23*	110 ± 24*†
	PEEP	98 ± 16	79 ± 22	94 ± 28*	151 ± 28*	151 ± 22	133 ± 17*	103 ± 12*†
	PEEP + volume	97 ± 19	95 ± 18	102 ± 20*	168 ± 18*	163 ± 21	140 ± 25*	107 ± 14*†
Cardiac output (l/min)	ZEEP	1.96 ± 0.27	1.77 ± 0.87	2.14 ± 1.12	3.08 ± 0.71*	1.79 ± 1.14*	1.61 ± 0.88	1.23 ± 0.41†
	ZEEP + volume	2.16 ± 0.28	1.82 ± 0.57	2.36 ± 0.79	3.87 ± 0.93*‡	3.08 ± 0.62*†	2.55 ± 0.66‡	2.03 ± 0.35‡
	PEEP	2.40 ± 0.90	1.07 ± 0.36*	1.21 ± 0.54‡§	1.40 ± 0.76*†§	2.12 ± 0.62*	2.54 ± 1.38‡	1.75 ± 0.44*†
	PEEP + volume	2.30 ± 0.61	1.17 ± 0.70*	1.51 ± 1.15§	2.51 ± 1.18*‡§	3.71 ± 1.26*‡#	3.65 ± 1.31‡§#	2.69 ± 0.91*‡#
Distal aortic pressure (mmHg)	ZEEP	—	15 ± 4	15 ± 3	14 ± 3	—	—	—
	ZEEP + volume	—	15 ± 2	15 ± 2	14 ± 2	—	—	—
	PEEP	—	16 ± 2	16 ± 2	15 ± 2	—	—	—
	PEEP + volume	—	16 ± 2	16 ± 2	16 ± 2	—	—	—
Mean pulmonary artery pressure (mmHg)	ZEEP	22 ± 5	24 ± 6	23 ± 5	22 ± 5	21 ± 3	21 ± 3	20 ± 5
	ZEEP + volume	22 ± 7	26 ± 9	27 ± 9	25 ± 6	22 ± 4	23 ± 4	21 ± 5
	PEEP	20 ± 6	29 ± 8*	27 ± 11	22 ± 3*	22 ± 5	23 ± 8	19 ± 7
	PEEP + volume	20 ± 6	28 ± 7*	28 ± 11	23 ± 2*	21 ± 7	21 ± 8	18 ± 4
Pulmonary artery wedge pressure (mmHg)	ZEEP	8 ± 1	10 ± 2*	11 ± 2	10 ± 2	10 ± 2	9 ± 2	9 ± 2
	ZEEP + volume	8 ± 1	11 ± 2*	13 ± 4	13 ± 2‡	9 ± 2*	9 ± 1	9 ± 1
	PEEP	8 ± 2	15 ± 3*‡§	14 ± 2‡	14 ± 2‡	9 ± 1*z	9 ± 1	8 ± 1
	PEEP + volume	7 ± 1	14 ± 2*‡§	13 ± 1‡	13 ± 2‡	9 ± 2*	10 ± 2	8 ± 2
Central venous pressure (mmHg)	ZEEP	6 ± 1	8 ± 1*	9 ± 2	7 ± 1	6 ± 2*	6 ± 1	6 ± 1
	ZEEP + volume	6 ± 1	8 ± 1*	9 ± 2	9 ± 2‡	5 ± 1*	6 ± 1*	6 ± 1
	PEEP	6 ± 1	11 ± 2*‡§	10 ± 1‡	10 ± 2‡	6 ± 2*	6 ± 2	5 ± 1
	PEEP + volume	6 ± 2	10 ± 1*‡§	11 ± 2‡§	12 ± 1‡§#	5 ± 1*	6 ± 2*	6 ± 2
Temperature (°C)	ZEEP	37.3 ± 0.7	37.2 ± 0.8	37.2 ± 0.8	37.2 ± 0.5	37.2 ± 0.6	37.2 ± 0.6	37.4 ± 0.7
	ZEEP + volume	37.4 ± 0.4	37.3 ± 0.4	37.3 ± 0.5	37.2 ± 0.4	37.1 ± 0.4	37.2 ± 0.3	37.3 ± 0.3
	PEEP	37.5 ± 0.5	37.4 ± 0.5	37.3 ± 0.5	37.1 ± 0.4	37.2 ± 0.3	37.2 ± 0.4	37.2 ± 0.4†
	PEEP + volume	37.2 ± 0.4	37.1 ± 0.4	37.1 ± 0.3	36.9 ± 0.3	37.1 ± 0.2	37.2 ± 0.2	37.3 ± 0.2
Systemic vascular resistance (dyne · s · cm^{-5})	ZEEP	3191 ± 710	6717 ± 3234*	5966 ± 2612	3894 ± 733*	2056 ± 739*	2789 ± 967	3164 ± 471
	ZEEP + volume	3235 ± 473	6740 ± 2368*	5170 ± 1644	3491 ± 1180*	1543 ± 449*	1963 ± 281	2633 ± 502
	PEEP	2943 ± 992	6687 ± 3086*	7260 ± 3770‡§	6864 ± 2612*‡§	2662 ± 850*	3034 ± 1559	2858 ± 1118
	PEEP + volume	3058 ± 634	7308 ± 2412*	7484 ± 4083‡§	5079 ± 3228*‡§	1894 ± 617*	2328 ± 727	2279 ± 776
Left ventricular stroke work (g × m)	ZEEP	22.5 ± 8.1	33.0 ± 14.3*	42.1 ± 24.0	37.4 ± 11.6	5.8 ± 4.6*	8.9 ± 7.0	8.1 ± 6.7†
	ZEEP + volume	26.9 ± 8.4	39.2 ± 16.3*	46.0 ± 21.4	50.5 ± 14.0‡	15.4 ± 7.5*‡	15.4 ± 7.6‡	17.1 ± 7.4
	PEEP	26.8 ± 14.7	14.9 ± 7.1*‡§	16.8 ± 11.2‡§	13.6 ± 8.9‡§	12.9 ± 5.8	19.6 ± 15.4*‡	13.8 ± 7.2*†
	PEEP + volume	27.8 ± 10.9	16.3 ± 13.0*‡§	21.7 ± 16.8‡§	25.7 ± 12.9§#	24.7 ± 11.9‡#	35.6 ± 13.8*‡§#	23.5 ± 8.6*
End-diastolic segment length (mm)	ZEEP	19.4 ± 4.8	20.1 ± 4.7*	20.2 ± 4.4	19.0 ± 4.9*	18.7 ± 5.2	19.2 ± 5.1	18.3 ± 4.7†
	ZEEP + volume	18.0 ± 5.1	19.2 ± 5.6*	18.9 ± 5.7	19.1 ± 5.3	18.3 ± 5.8	18.7 ± 5.7	18.8 ± 5.4
	PEEP	19.6 ± 3.7	19.3 ± 3.3	19.3 ± 3.8	18.4 ± 3.5*	18.3 ± 3.7	19.0 ± 3.8*	19.0 ± 3.4†
	PEEP + volume	19.6 ± 4.1	19.2 ± 4.2	19.1 ± 3.9	18.7 ± 3.7	18.9 ± 4.0	19.4 ± 4.2*	19.7 ± 4.2
End-systolic segment length (mm)	ZEEP	17.2 ± 4.8	18.2 ± 4.1*	18.2 ± 3.9	17.3 ± 4.7*	17.2 ± 4.9	17.9 ± 4.8	17.4 ± 5.0
	ZEEP + volume	16.1 ± 4.6	17.2 ± 4.8*	16.9 ± 4.9	17.4 ± 4.7	16.6 ± 5.4	17.1 ± 5.4	17.7 ± 5.5
	PEEP	17.5 ± 3.1	17.3 ± 3.3	17.5 ± 3.5	17.1 ± 3.6	16.5 ± 3.0	17.2 ± 3.3*	17.4 ± 3.0
	PEEP + volume	17.5 ± 4.3	17.2 ± 4.3	17.1 ± 3.8	17.1 ± 3.6	16.8 ± 3.7	17.5 ± 3.6*	17.9 ± 3.9
Segmental shortening (%)	ZEEP	11.7 ± 3.4	9.5 ± 1.9	10.1 ± 3.8	8.9 ± 3.5	8.2 ± 3.9	7.1 ± 2.6	5.6 ± 3.2†
	ZEEP + volume	10.6 ± 3.2	10.2 ± 4.1	10.2 ± 4.1	8.7 ± 3.5	9.5 ± 2.4	8.3 ± 4.4	6.3 ± 3.2†
	PEEP	10.5 ± 2.7	10.2 ± 4.9	9.4 ± 5.2	7.6 ± 3.9	9.5 ± 4.2	8.8 ± 3.6	8.5 ± 3.1
	PEEP + volume	10.3 ± 2.6	10.8 ± 5.3	10.3 ± 4.5	9.1 ± 3.3	11.2 ± 4.0	9.6 ± 3.6	9.3 ± 3.0

* $P < 0.005$ compared with previous value. † $P < 0.005$ compared with baseline. ‡ $P < 0.005$ compared with ZEEP. § $P < 0.005$ compared with ZEEP + volume. # $P < 0.005$ compared with PEEP.

ZEEP = zero end-expiratory pressure; PEEP = positive end-expiratory pressure.

The hemodynamic response to acute aortic occlusion is characterized by an increase in systemic vascular resistance and mean aortic blood pressure with variable effects on LV stroke volume and cardiac filling pressures.[6] Multiple factors influence the magnitude of cardiac load and include (1) an increase in LV afterload secondary to greater aortic impedance[19] and humoral changes in the renin–angiotensin system;[20] (2) alterations in preload from blood volume redistribution;[21,22] (3) a change in coronary hydraulic properties, which can reduce myocardial compliance;[23] and (4) underlying myocardial performance, specifically the sensitivity of LV pump function to acute alterations in preload and afterload. In patients with coexisting ventricular contrac-

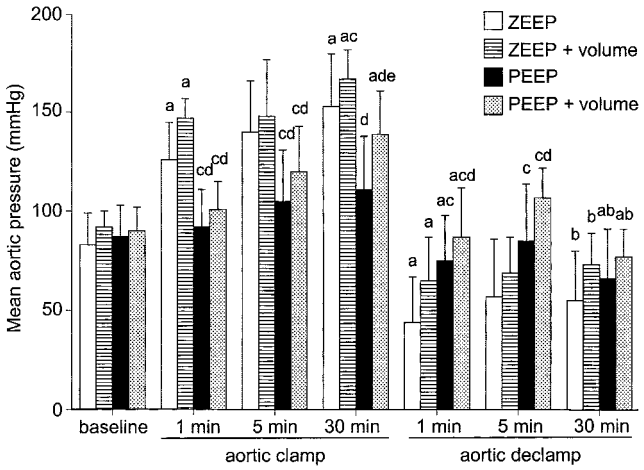

Fig. 1. Mean aortic pressure increased after cross-clamp application in both zero end-expiratory pressure (ZEEP) groups but remained significantly lower in both positive end-expiratory pressure (PEEP) groups at 1 and 5 min. Although volume administration further increased mean aortic pressure, mean aortic pressure remained lower in respective groups treated with PEEP. After cross-clamp removal, mean aortic pressure decreased in all groups while remaining highest in the PEEP + volume group; these changes persisted at 1 and 5 min. Thirty minutes after declamping, aortic pressure was comparable in all groups but lower than baseline. (*A* indicates $P < 0.005$ compared with previous adjacent value within the group; *B* indicates $P < 0.005$ compared with baseline value within the group; *C* indicates $P < 0.005$ compared with ZEEP animals; *D* indicates $P < 0.005$ compared with ZEEP + volume animals; *E* indicates $P < 0.005$ compared with PEEP animals).

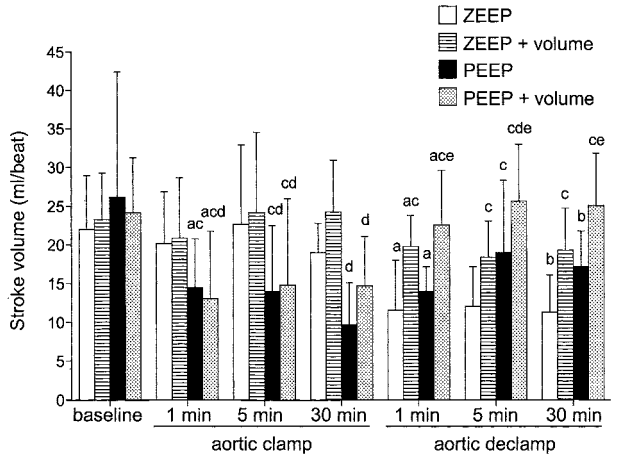

Fig. 2. After cross-clamp application, stroke volume decreases in both positive end-expiratory pressure (PEEP) groups but not with zero end-expiratory pressure (ZEEP). Subsequent volume administration tended to maintain stroke volume during cross-clamp. However, after cross-clamp release, stroke volume increased in both PEEP groups and was highest in the PEEP + volume group. During reperfusion, stroke volume remained similar in PEEP and ZEEP + volume groups. (*A* indicates $P < 0.005$ compared with previous adjacent value within the group; *B* indicates $P < 0.005$ compared with baseline value within the group; *C* indicates $P < 0.005$ compared with ZEEP animals; *D* indicates $P < 0.005$ compared with ZEEP + volume animals; *E* indicates $P < 0.005$ compared with PEEP animals).

tile dysfunction and limited preload-recruitable function, an acute increase in LV afterload could cause a marked decrease in stroke volume, in turn causing ventricular dilation[4] and ensuing ischemic changes.[2] In animal studies of supraceliac aortic cross-clamp, preload increases secondary to splanchnic venous collapse from elastic recoil and reduced venous volume.[21,22] Our data with ZEEP animals confirm this finding, with a significant increase in LV end-diastolic segment length after aortic cross-clamping. The application of PEEP prevents an increase in end-diastolic segment length, although filling pressures were greater presumably the result of transmitted intrathoracic pressure. In fact, PEEP during aortic cross-clamp produces similar hemodynamic effects as described in the experimental model with simultaneous occlusion of the aorta plus inferior vena cava.[24,25] Whereas occlusion of the descending thoracic aorta in dogs causes a net transfer of blood volume to the upper body, occlusion of aorta and inferior vena cava causes blood redistribution to the lower body without a concomitant increase in systolic arterial pressure.[24] It is possible that, by impeding venous return to the right heart and increasing splanchnic venous volume, PEEP works in a similar yet more controllable manner.

Although perfusion distal to the cross-clamp appears proportionate to proximal aortic pressure,[10] the increase in systolic pressure with cross-clamp application represents a true afterload experienced by the heart and can interfere with secure placement of the cross-clamp. Consequently, some control of proximal blood pressure may be required during aortic surgery. Therapeutic measures to reduce or minimize the hemodynamic consequences of acute aortic occlusion include the titration of vasodilator drugs, volatile anesthetic agents, and hemodilution. Volatile anesthetic agents effectively reduce aortic pressure but have the distinct disadvantage of depressing myocardial contractility with persistent effects after declamping. Vasodilators, such as nitroglycerin, have a predominant preload-reducing rather than afterload-reducing effect; PEEP produces a similar hemodynamic profile. However, clinical experience with nitroglycerin shows an increase in cardiac output and mixed venous oxygen saturation during cross-clamping,[8] whereas the addition of PEEP in our study further reduces cardiac output by nearly 50%. Nevertheless, because nearly half the body is excluded by the aortic clamp, the decrease in cardiac output by PEEP does not adversely affect arterial pH or base deficit when compared with ZEEP animals. Vasodilators, such as nitroprusside, are effective to reduce blood pressure during aortic occlusion but can further reduce distal aortic pressure, visceral perfusion, and oxygen consumption.[10] In our study, PEEP does not adversely affect distal perfusion pressure measured below the cross-clamp, although further study is required to examine regional visceral perfusion with the addition of PEEP.

Aortic declamping causes significant hypotension secondary to the precipitous reduction in vascular resistance, sequestration of blood volume in the distal capillary beds, and negative inotropic effect from acidosis and

Table 2. Oxygenation Variables throughout the Experimental Procedure

Variable	Group	Baseline	Aortic Clamp			Aortic Declamp		
			1 min	5 min	30 min	1 min	5 min	30 min
Serum hemoglobin (g/dl)	ZEEP	11.3 ± 1.7	11.3 ± 1.1	11.4 ± 1.1	12.6 ± 1.2*	13.6 ± 1.1*	13.6 ± 1.7	12.8 ± 1.4†
	ZEEP + volume	11.7 ± 1.3	11.4 ± 1.0	10.9 ± 1.6	10.4 ± 1.3*‡	11.4 ± 1.6*‡	11.5 ± 1.4‡	11.0 ± 1.3‡
	PEEP	11.6 ± 1.9	11.6 ± 1.7	11.6 ± 1.6	12.2 ± 2.0*§	13.4 ± 2.2*§	13.4 ± 2.4§	13.0 ± 2.7†§
	PEEP + volume	11.3 ± 1.7	11.3 ± 1.7	10.6 ± 1.1	9.4 ± 1.1*‡#	11.4 ± 1.4*‡#	11.5 ± 1.5‡#	10.4 ± 1.0‡#
*p*H	ZEEP	7.44 ± 0.04	7.46 ± 0.05	7.49 ± 0.06	7.42 ± 0.06*	7.22 ± 0.07*	7.25 ± 0.08*	7.29 ± 0.06*†
	ZEEP + volume	7.44 ± 0.04	7.48 ± 0.05	7.47 ± 0.05	7.38 ± 0.06*	7.18 ± 0.07*	7.27 ± 0.08*	7.33 ± 0.05*†
	PEEP	7.44 ± 0.05	7.50 ± 0.07*	7.52 ± 0.08	7.46 ± 0.09*	7.16 ± 0.08*	7.24 ± 0.08*	7.32 ± 0.06*†
	PEEP + volume	7.45 ± 0.03	7.54 ± 0.04*	7.54 ± 0.05	7.44 ± 0.07*	7.16 ± 0.07*	7.30 ± 0.05*	7.35 ± 0.05*†
$Paco_2$ (mmHg)	ZEEP	40 ± 4	37 ± 4	35 ± 4	36 ± 5	51 ± 10*	46 ± 6*	41 ± 3*
	ZEEP + volume	40 ± 4	36 ± 4	37 ± 5	39 ± 4	56 ± 6*	44 ± 5*	41 ± 4
	PEEP	39 ± 3	34 ± 4*	31 ± 4	33 ± 6	57 ± 7*	46 ± 6*	40 ± 4*
	PEEP + volume	39 ± 2	32 ± 4*	31 ± 4	36 ± 8	60 ± 9*	42 ± 5*	39 ± 4
Pao_2 (mmHg)	ZEEP	275 ± 124	316 ± 87	339 ± 137	306 ± 139	182 ± 86*	250 ± 115*	256 ± 132
	ZEEP + volume	317 ± 56	323 ± 50	320 ± 77	324 ± 86	222 ± 93*	309 ± 92*	299 ± 45
	PEEP	269 ± 102	303 ± 87	316 ± 94	323 ± 128	225 ± 97*	272 ± 112*	289 ± 101
	PEEP + volume	353 ± 123	337 ± 81	383 ± 106	361 ± 106	264 ± 111*	300 ± 84*	348 ± 97
Arterial bicarbonate tension (mmHg)	ZEEP	27.3 ± 1.5	27.2 ± 1.9	27.1 ± 1.7	23.9 ± 1.3*	21.7 ± 2.6*	20.2 ± 2.8*	20.3 ± 2.1*†
	ZEEP + volume	27.1 ± 1.9	26.7 ± 1.9	26.6 ± 1.7	23.0 ± 1.9*	21.6 ± 3.0*	20.4 ± 2.2*	21.4 ± 2.9*†
	PEEP	26.9 ± 2.3	26.8 ± 2.5	25.8 ± 3.0	23.4 ± 2.4*	20.1 ± 2.5*	19.2 ± 1.7*	20.7 ± 2.0*†
	PEEP + volume	27.1 ± 1.6	27.0 ± 1.2	26.4 ± 1.2	24.0 ± 1.6*	21.9 ± 2.2*	20.7 ± 1.5*	21.6 ± 1.5*†
Base deviation (mg/l)	ZEEP	3.7 ± 1.7	3.9 ± 2.1	4.2 ± 2.2	0.2 ± 8.7*	−5.0 ± 2.9*	−5.3 ± 3.3	−5.1 ± 2.8†
	ZEEP + volume	3.4 ± 2.2	3.8 ± 2.3	3.3 ± 1.9	−1.2 ± 2.4*	−5.6 ± 3.7*	−5.3 ± 3.1	−3.5 ± 3.4†
	PEEP	3.2 ± 2.9	4.2 ± 2.8	3.7 ± 3.5	0.5 ± 3.1*	−7.1 ± 3.2*	−6.5 ± 2.5	−3.4 ± 3.5*†
	PEEP + volume	3.5 ± 1.7	4.8 ± 1.4	4.3 ± 1.4	0.6 ± 1.3*	−5.8 ± 2.4*	−4.8 ± 1.5	−3.0 ± 1.9*†

* $P < 0.005$ compared with previous value. † $P < 0.005$ compared with baseline value. ‡ $P < 0.005$ compared with ZEEP value. § $P < 0.005$ compared with ZEEP + volume value. # $P < 0.005$ compared with PEEP.

ZEEP = zero end-expiratory pressure; PEEP = positive end-expiratory pressure.

myocardial depressant factors.[6,11,14] The potential for hypovolemia may be worsened by intravascular fluid loss caused by capillary damage with reperfusion.[6,10] The amount of ensuing hypovolemia during declamping can be attenuated by volume expansion before clamp release;[11–14] volume expansion after aortic cross-clamp release is less effective. However, limitations on volume expansion include arterial hypertension during cross-clamp application and the potential to prolong postoperative recovery.[26] Similar benefit is found with volume expansion in ZEEP animals, although higher aortic blood pressures are seen during cross-clamp application.

Because of its rapid onset, short half-life, and ability to be titrated, PEEP could offer particular advantages with the abrupt swings in loading conditions inherent to major aortic surgery. PEEP produces multiple effects on ventricular loading conditions. In experimental animals, PEEP reduces venous return and right ventricular preload, although the exact mechanisms remain somewhat unclear.[15,27] PEEP increases intrathoracic pressure, which could reduce transmural filling pressure. However, the net pressure gradient for venous return to the right heart does not change with PEEP because of simultaneous increases in intraabdominal and systemic back pressures.[27,28] Other potential mechanisms include inferior vena caval compression by lung hyperinflation[27] and an increase in splanchnic venous resistance by mechanical compression from diaphragmatic descent.[28] Similarly, PEEP can reduce LV transmural ejection pressure, defined as the difference between LV developed pressure and pericardial pressure, and, consequently, LV afterload.[16] PEEP can also reduce LV compliance. Specifically, in the splanchnic circulation, PEEP causes passive venous distention with blood sequestration;[29] these effects could counteract the splanchnic venous collapse and blood redistribution associated with supraceliac aortic occlusion.[21,22] In our study, intravascular volume appears to be preserved better with PEEP, which produces the same hemodynamic benefit during declamping as volume expansion in ZEEP animals. Accordingly, the greatest benefit occurred with PEEP + volume expansion, where stroke volume with declamping was double that seen with ZEEP alone.

A potential drawback to this study is the use of animals having normal ventricular function. Positive airway pressure produces greater hemodynamic benefit in patients with left heart failure and afterload sensitivity than in healthy patients.[30] Anecdotally, we have used 7.5–12.5 cm H_2O PEEP in several patients undergoing aortic aneurysmectomy who have a reduced ejection fraction resulting from ischemic heart disease. Our clinical experience with these patients indicates that PEEP allows more precise hemodynamic control and permits volume expansion and the administration of inotropic drugs (*e.g.*, dobutamine) during aortic occlusion with less declamp hypotension after clamp removal. Further study

is necessary in an animal model of congestive failure to substantiate this clinical impression of PEEP. In addition, other factors should be considered when using PEEP therapy in patients. Our animals did not have underlying coronary artery disease, which could independently affect the response to PEEP. PEEP may worsen left[31] and right[32] ventricular ischemic injury, and this possibility should be considered when using PEEP in patients with vascular disease. PEEP can increase pulmonary vascular resistance and right ventricular oxygen demands,[32] which may be detrimental in patients with severe underlying pulmonary disease. Second, the changes in stroke volume in our study do not correlate well with LV free wall segment lengths. Besides any obvious discrepancy that may exist between right- and left-sided events associated with PEEP and aortic cross-clamp, a limited number and position of dimension transducers were used in our study to minimize alterations in pericardial integrity. Examining a greater number of dimensions may allow a more detailed and sensitive reflection of changes in LV volume, particularly with the noncongruent changes in ventricular geometry reported with PEEP.[33]

In conclusion, 15 cm H_2O PEEP attenuates the hypertensive response to acute aortic occlusion in pigs and allows concomitant volume expansion. During subsequent declamping, the abrupt discontinuation of PEEP causes less hypotension than with ZEEP. Although volume expansion during cross-clamp directly improves stroke volume with declamping, the greatest improvement in stroke volume and aortic blood pressure was found in PEEP + volume–treated animals. The use of PEEP may be beneficial in patients during acute aortic clamping and declamping.

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References

1. Schuetz W, Radermacher P, Goertz A, Georgieff M, Gauss A: Cardiac function in patients with treated hypertension during aortic aneurysm repair. J Cardiothorac Vasc Anesth 1998; 12:33–7

2. Attia RR, Murphy JD, Snider M, Lappas DG, Darling RC, Lowenstein E: Myocardial ischemia due to infrarenal aortic cross-clamping during aortic surgery in patients with severe coronary artery disease. Circulation 1976; 53:961–5

3. Gooding JM, Archie JP, McDowell H: Hemodynamic response to infrarenal aortic cross-clamping in patients with and without coronary artery disease. Crit Care Med 1980; 8:382–5

4. Roizen MF, Beaupre PN, Alpert RA, Kremer P, Cahalan MK, Shiller N, Sohn YJ, Cronnelly R, Lurz FW, Ehrenfeld WK: Monitoring with two-dimensional transesophageal echocardiography. Comparison of myocardial function in patients undergoing supraceliac, suprarenal-infraceliac, or infrarenal aortic occlusion. J Vasc Surg 1984; 1:300–5

5. Sprung J, Abdelmalak B, Gottlieb A, Mayhew C, Hammel J, Levy PJ, O'Hara P, Hertzer NR: Analysis of risk factors for myocardial infarction and cardiac mortality after major vascular surgery. ANESTHESIOLOGY 2000; 93:129–40

6. Gelman S: The pathophysiology of aortic cross-clamping and unclamping. ANESTHESIOLOGY 1995; 82:1026–60

7. Poli de Figueiredo LF, Mathru M, Tao W, Solanki D, Uchida T, Kramer GC: Hemodynamic effects of isovolemic hemodilution during descending thoracic aortic cross clamping and lower torso reperfusion. Surgery 1997; 122:32–8

8. Zaidan JR, Guffin AV, Perdue G, Smith R, McNeill DC: Hemodynamics of intravenous nitroglycerin during aortic clamping. Arch Surg 1982; 117:1285–8

9. Gelman S, Reves JG, Fowler K, Samuelson PN, Lell WA, Smith LR: Regional blood flow during cross-clamping of the thoracic aorta and infusion of sodium nitroprusside. J Thorac Cardiovasc Surg 1983; 85:287–91

10. Gregoretti S, Gelman S, Henderson T, Bradley EL: Hemodynamics and oxygen uptake below and above aortic occlusion during crossclamping of the thoracic aorta and sodium nitroprusside infusion. J Thorac Cardiovasc Surg 1990; 100:830–6

11. Baue AE, McClerkin WW: A study of shock: Acidosis and the declamping phenomenon. Ann Surg 1965; 161:41–5

12. Bush HL, LoGerfo FW, Weisel RD, Mannick JA, Hechtman HB: Assessment of myocardial performance and optimal volume loading during elective abdominal aortic aneurysm resection. Arch Surg 1977; 112:1301–5

13. Lunn JK, Dannemiller FJ, Stanley TH: Cardiovascular responses to clamping of the aorta during epidural and general anesthesia. Anesth Analg 1979; 58:372–6

14. Reiz S, Peter T, Rais O: Hemodynamic and cardiometabolic effects of infrarenal aortic and common iliac artery declamping in man—An approach to optimal volume loading. Acta Anaesthesiol Scand 1979; 23:579–86

15. Johnston WE, Vinten-Johansen J, Santamore WP, Case LD, Little WC: Mechanism of reduced cardiac output during positive end-expiratory pressure in the dog. Am Rev Respir Dis 1989; 140:1257–64

16. Pinsky MR, Matuschak GM, Klain M: Determinants of cardiac augmentation by elevations in intrathoracic pressure. J Appl Physiol 1985; 58:1189–98

17. Husby P, Heltne JK, Koller ME, Birkeland S, Westby J, Fosse R, Lund T: Midazolam-fentanyl-isoflurane anaesthesia is suitable for haemodynamic and fluid balance studies in pigs. Lab Anim 1998; 32:316–23

18. Hoit BD, Lew WY: Functional consequences of acute anterior vs. posterior wall ischemia in canine left ventricles. Am J Physiol 1988; 254:H1065–73

19. Johnston WE, Balestrieri FJ, Plonk G, D'Souza V, Howard G: The influence of periaortic collateral vessels on the intraoperative hemodynamic effects of acute aortic occlusion in patients with aorto-occlusive disease or abdominal aortic aneurysm. ANESTHESIOLOGY 1987; 66:386–9

20. Roytblat L, Gelman S, Henderson T, Bradley E: Humoral factors and hemodynamics during cross-clamping of the thoracic aorta. J Cardiothorac Vasc Anesth 1991; 5:10–4

21. Stokland O, Molaug M, Thorvaldson J, Ilebekk A, Kiil F: Cardiac effects of splanchnic and non-splanchnic blood volume redistribution during aortic occlusions in dogs. Acta Physiol Scand 1981; 113:139–46

22. Gelman S, Khazaeli MB, Orr R, Henderson T: Blood volume redistribution during cross-clamping of the descending aorta. Anesth Analg 1994; 78:219–24

23. Gilbert JC, Glantz SA: Determinants of left ventricular filling and of the diastolic pressure- volume relation. Circ Res 1989; 64:827–52

24. Stokland O, Miller MM, Ilebekk A, Kiil F: Mechanism of hemodynamic responses to occlusion of the descending thoracic aorta. Am J Physiol 1980; 238:H423–9

25. Gelman S, Rabbani S, Bradley EL: Inferior and superior vena caval blood flows during cross-clamping of the thoracic aorta in pigs. J Thorac Cardiovasc Surg 1988; 96:387–92

26. Bertges DJ, Rhee RY, Muluk SC, Trachtenberg JD, Steed DL, Webster MW, Makaroun MS: Is routine use of the intensive care unit after elective infrarenal abdominal aortic aneurysm repair necessary? J Vasc Surg 2000; 32:634–42

27. Fessler HE, Brower RG, Wise RA, Permutt S: Effects of positive end-expiratory pressure on the canine venous return curve. Am Rev Respir Dis 1992; 146:4–10

28. Brienza N, Revelly JP, Ayuse T, Robotham JL: Effects of PEEP on liver arterial and venous blood flows. Am J Respir Crit Care Med 1995; 152:504–10

29. Risoe C, Hall C, Smiseth OA: Splanchnic vascular capacitance and positive end-expiratory pressure in dogs. J Appl Physiol 1991; 70:818–24

30. Naughton MT, Rahman MA, Hara K, Floras JS, Bradley TD: Effect of continuous positive airway pressure on intrathoracic and left ventricular transmural pressures in patients with congestive heart failure. Circulation 1995; 91:1725–31

31. Tittley JG, Fremes SE, Weisel RD, Christakis GT, Evans PJ, Madonik MM, Ivanov J, Teasdale SJ, Mickle DA, McLaughlin PR: Hemodynamic and myocardial metabolic consequences of PEEP. Chest 1985; 88:496–502

32. Johnston WE, Vinten-Johansen J, Shugart HE, Santamore WP: Positive end-expiratory pressure potentiates the severity of canine right ventricular ischemia-reperfusion injury. Am J Physiol 1992; 262:H168–76

33. Bell RC, Robotham JL, Badke FR, Little WC, Kindred MK: Left ventricular geometry during intermittent positive pressure ventilation in dogs. J Crit Care 1987; 2:230–44