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Effect of positive end-expiratory pressure on splanchnic perfusion in acute lung injury

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Abstract *Objective*: To evaluate the acute effects of an increased positive end-expiratory pressure (PEEP) on splanchnic tissue perfusion.
Design: Clinical prospective study.
Setting: Intensive care unit in a university clinic.
Patients: Six patients with severe acute lung injury (ALI) requiring mechanical ventilation. All patients had bilateral infiltrates in chest X-ray, PaO_2/FiO_2 < 200 mmHg and stable hemodynamics without vasoactive drugs.
Interventions: PEEP was increased by 5 cmH_2O from a clinically selected PEEP level (8/6–11 cmH_2O) up to (13/10–14 cmH_2O) followed by a return to baseline.
Measurements and main results: Splanchnic blood flow was measured using primed continuous infusion of indocyanine green dye with hepatic venous sampling and systemic hemodynamics by routine monitoring. In addition, we estimated gastric mucosal-arterial PCO_2 difference and splanchnic lactate/pyruvate exchange. After a baseline measurement, PEEP was increased. After 60 min all measurements were repeated. PEEP was returned to the baseline level and a third measurement followed. PEEP had no effect on cardiac index (baseline I: 3.2/6.1–2.5 l/min/m^2; PEEP: 3.3/5.7–2.3 l/min/m^2; baseline II: 3.4/6.0–2.5 l/min/m^2); neither did PEEP have any effect on splanchnic blood flow (baseline I: 0.91/1.39–0.62 l/min/m^2; PEEP: 1.04/1.75–0.54 l/min/m^2; baseline II:1.07/1.42–0.68 l/min/m^2, respectively) or perfusion (gastric mucosal-arterial PCO_2 difference baseline I: 2.1/12.8–0.6 kPa; PEEP: 1.7/14.5–0.7 kPa; baseline II: 1.7/8.8–0.1 kPa; lactate uptake baseline I: 0.5/1.1–0.3 mmol/min/m^2; PEEP: 0.4/1.0–0.3 mmol/min/m^2; baseline II: 0.5/0.9–0.3 mmol/min/m^2; hepatic venous lactate/pyruvate baseline I: 9.7/10.6–5.7; PEEP: 9.7/14.2–6.4; baseline II: 8.4/12.4–7.3; respectively).
Conclusion: PEEP by itself does not have a consistent effect on splanchnic blood flow and metabolism when cardiac index is stable and patients are ventilated within the linear part of the pv curve.

Key words Acute lung injury · Pressure gradients · PEEP · Splanchnic perfusion

Introduction

The use of positive end-expiratory pressure (PEEP) is an established component of the mechanical ventilatory support of the acute respiratory distress syndrome (ARDS) [1, 2, 3]. PEEP helps to improve arterial oxygenation and restore functional residual capacity, but it also has important circulatory side effects. The increase in intrathoracic pressures may decrease venous return and cardiac output, and oxygen delivery may in

Table 1 Parameters of respiratory function. *PEEPtot* = total PEEP; *VT* = tidal volume

	Total compliance		Parameters of respiratory function								
	Baseline ml/cm H_2O	PEEP ml/cm H_2O	Age	PaO_2/FiO_2	FiO_2	Resp. Fr./min	VT ml	PEEPset Baseline cm H_2O	PEEPtot Baseline cm H_2O	PEEPset PEEP cm H_2O	PEEPtot PEEP cm H_2O
Pat. 1	42	38	70	145	0.4	13	665	6	7	11	12
Pat. 2	59	68	65	156	0.4	16	685	5	6	10	10
Pat. 3	49	50	67	200	0.4	20	570	5	10	10	13
Pat. 4	50	55	50	197	0.4	15	665	8	8	13	13
Pat. 5	63	65	67	161	0.4	14	625	6	11	11	14
Pat. 6	47	51	47	146	0.5	21	560	8	8	13	13

fact decrease despite improved arterial oxygenation [4, 5, 6].

Furthermore, application of PEEP may reduce cardiac output and influence its distribution [4, 6, 7, 8, 9]. Marked reduction of total hepatic and portal venous blood flow has been reported in various experimental models, but the results are controversial [10, 11, 12, 13, 14]. Splanchnic tissue perfusion may therefore be at risk in patients with acute lung injury (ALI) and ARDS, and impaired splanchnic tissue perfusion may contribute to increased morbidity and mortality in patients requiring mechanical ventilation [15, 16, 17]. It is possible that despite an improved PaO_2, PEEP may in fact reduce regional oxygen delivery by decreased splanchnic blood flow and tissue perfusion.

In patients without ALI, perioperative application of PEEP reduced splanchnic blood flow [18, 19, 20]. The effects of PEEP on splanchnic blood flow and tissue perfusion**,** however, have not been studied in patients with ALI. In experimental models, increased intrathoracic pressure due to application of PEEP has been considered a main reason for reduced splanchnic blood flow [9, 11]. In clinical ALI the effect of increased airway pressure on splanchnic blood flow may be modified due to reduced transmission of airway pressure to intrathoracic and intraabdominal vessels and due to heart-lung interaction [9]. In addition, the effects of PEEP on inspiratory lung volume and pressure may further modify the effects on both systemic and regional blood flow.

Therefore, we hypothesized that in clinical ALI the effects of PEEP on splanchnic blood flow and metabolism may be different from those observed in experimental models or intraoperative patients, especially when ventilation is titrated in the linear part of the pv-curve. The aim of this study was to clarify the mechanisms regarding how clinically relevant levels of PEEP influence the total hepatosplanchnic blood flow, venous driving pressures and various indices of gastrointestinal tissue perfusion and metabolism in patients with severe ALI.

Materials and methods

The study was approved by the Ethics Committee of the Kuopio University Hospital and written informed consent was obtained from the family of each patient. The six patients studied had ALI according to the following criteria: (1) acute bilateral infiltrates in the chest radiograph; (2) known etiology of ALI; (3) $PaO_2/FiO_2 < 200$ mmHg, $PaCO_2$ 32–46 mmHg; (4) no cardiogenic cause of lung edema; (5) mechanical ventilation due to ALI. In addition they fulfilled the following criteria: (1) age 18–70 y; (2) mean systemic arterial pressure 60–110 mmHg; (3) no vasoactive drugs in use and cardiac index > 2.5 l/min/m^2; (4) arterial blood lactate < 2.5 mmol/l, hemoglobin > 100 g/l. The etiology of ALI was pneumonia in five patients and one patient developed ALI after peritonitis.

The patients were ventilated in a volume-controlled mode with an inspiratory time of 30 %–50 %, PEEP levels between 4–10 cmH_2O, tidal volume of 5–10 ml/kg and an inspiratory pressure < 35 cmH_2O according to clinical debits (Table 1). None of the patients had a preexisting liver disease. None of the patients had clinically or biochemically evident liver dysfunction and they had relatively well-preserved indocyanine green extraction (57 ± 22 %; mean ± SD) (Table 2).

Protocol

Before the baseline measurement of gas exchange and systemic and regional blood flow, gas exchange and hemodynamics were monitored for 60 min to assure a stable clinical condition. During this period, no changes were made in the ventilator settings or other treatment. Following the 60 min stabilization the hepatosplanchnic blood flow was measured during the next 30 min, and data were collected for systemic and splanchnic hemodynamics, gas exchange and respiratory mechanics. After the baseline measurement, the PEEP set in the ventilator was increased by 5 cmH_2O. After 60 min of stabilization, the regional blood flow measurement and collection of other data were repeated during a 30 min period, and PEEP was then reduced to the baseline level. Again after 60 min of stabilization, the regional blood flow measurement and collection of other data were repeated. The total duration of the study was 270 min.

All studies were accomplished during volume controlled mechanical ventilation (Servo 900 C, Siemens, Solna, Sweden), and the patients were sedated with midazolam (Dormicum, Hoffmann LaRoche, Basel, Switzerland) and paralyzed with pancuronium (Pavulon, N. V. Organon, Oss, The Netherlands). During the protocol the patients were not fed enterally. None of the patients re-

Table 2 Global hemodynamics

	Systemic Hemodynamics		
	Baseline	Increased PEEP	Baseline
Cardiac index l/min/m^2	3.1 (5.5–2.5)	3.2 (4.6–2.3)	3.2 (5.2–2.5)
Heart rate str./min	95 (112–89)	95 (103–91)	97 (99–90)
Mean arterial pressure mm Hg	67 (94–57)	76 (87–61)	70 (91–51)
Mean pulmonary arterial pressure mm Hg	22 (35–16)	23 (34–17)	22 (35–16)
Central venous pressure mm Hg	7 (9–5)	8 (10–6)[a]	7 (9–5)[b]
Pulmonary arterial occlusion pressure mm Hg	8 (13–4)	10 (16–7)	9 (15–7)
Venous admixture %	33 (45–18)	28 (40–12)	30 (38–13)
Oxygen delivery ml/min/m^2	438 (780–360)	420 (704–299)	430 (761–330)
Oxygen consumption ml/min/m^2	131 (167–95)	128 (164–89)	126 (170–94)
Carbondioxide production ml/min/m^2	115 (134–71)	109 (139–79)	113 (134–77)
Arterial partial oxygen pressure kPa	8.2 (10.8–7.3)	9.9 (10.8–8.7)[a]	9.2 (11.9–8.0)

*$P < 0.05$ vs baseline

ceived any therapeutic intervention of hemodynamics during the study (volume loading, vasoactive drugs). In addition to the catheters for routine monitoring (radial and pulmonary artery catheters), a catheter was inserted in the hepatic vein. The hepatic vein was cannulated via the right internal jugular vein, and the correct position of the catheter was verified before and after the study by fluoroscopy using a small amount of contrast dye.

A nasogastric tube (TRIP NGS Catheter; Tonometrics, Worcester, Mass., USA) was inserted in the stomach [21, 22].

Regional blood flow measurement

The total hepatosplanchnic blood flow was estimated by a primed, continuous infusion of indocyanine green, based on the Fick principle and hepatic venous sampling [23, 24], as described previously. Briefly, the indocyanine green method measures total hepatosplanchnic blood flow, that is, the sum of both portal venous and hepatic arterial blood flow. After a priming dose of indocyanine green 12 mg, a constant infusion of 1.1 mg/min^{-1} was continued for 30 min. Blood samples were obtained simultaneously from the hepatic vein and an artery. Splanchnic blood flow was calculated as follows:

splanchnic blood flow index = infusion rate × Ci/(Ca-Chv) × (1–Hcr) where Ci = indocyanine green concentration of the infusate, Ca and Chv = indocyanine green concentrations in the artery and hepatic vein, respectively, and Hcr = hematocrit.

Indocyanine green extraction was 57 ± 22 % (mean ± SD), exceeding in each single measurement the limit of 10 %, which is required for valid application of this method [25]. The coefficients of variation for consecutive blood flow measurements at 20, 25 and 30 min during each infusion of indocyanine green was 5 ± 4 % (mean ± SD).

In addition to the systemic and splanchnic hemodynamics we also recorded the hepatic venous pressure (HVP) as well as the hepatic venous occlusion pressure (HVOP), an estimate of the portal venous pressure [26, 27]. The HVOP enabled us to estimate selectively the changes in driving pressures of venous return in the prehepatic and the hepatic region. The HVOP was estimated by inflating the balloon of the Swan-Ganz-catheter positioned in the hepatic vein.

Other measurements

Oxygen consumption (VO_2) and carbon dioxide production (VCO_2) were measured continuously from the inspired and expired respiratory gases by open-circuit indirect calorimetry (Deltatrac, Datex/Instrumentarium, Helsinki, Finland). The calorimetry device has been validated in this laboratory [28]. The oxygen extraction was calculated as the arterial-mixed venous oxygen content difference/arterial oxygen content. Cardiac output was measured by thermodilution in triplicate using 10 ml of room temperature saline solution before the blood sampling at 20 min and after the sampling at 30 min, and the mean value was used for the calculations. Cardiac output was also measured according to Fick's principle, using the measured VO_2 and the difference between arterial and venous oxygen contents. The mean of the thermodilution and Fick cardiac output was used for analyses. This was done in order to achieve the best possible estimate of cardiac output corresponding to the whole sampling period for splanchnic blood flow measurement. Oxygen delivery (DO_2) was calculated as the product of thermodilution cardiac output and arterial oxygen content (CaO_2). The global oxygen extraction was calculated as VO_2/DO_2. Regional DO_2 was calculated as the product of regional flow and CaO_2. Regional oxygen extraction was calculated as arterial-hepatic venous oxygen content difference/arterial oxygen content, and the regional VO_2 as the product of the hepatosplanchnic blood flow and the arterial-hepatic venous oxygen content difference.

Blood samples were taken simultaneously with the blood flow measurement from the artery and the hepatic vein for the measurement of blood lactate and pyruvate concentrations, and blood gases. The plasma lactate (YSI, 2300 Stat plus Lactate Analyser, Yellow Springs, Ohio, USA) and the pyruvate concentrations (Sigma UV, Sigma Diagnostics, St. Louis, Mo., USA) were measured enzymatically. Regional lactate uptake and release were calculated as the product of the regional blood flow and the difference between arterial and venous lactate concentrations. Blood gases and oxygen contents were measured using a clinical blood gas analyzer (ABL-500, Radiometer, Copenhagen, Denmark) and a co-oximeter (OSM-3, Radiometer, Copenhagen, Denmark). For the gastric tonometry, the saline samples were equilibrated for 90 min and the last 30 min corresponding to the period of the indocyanine green infusion. The $PaCO_2$ of the saline was always measured with the same blood gas analyzer immediately after sampling [22], and the measured value was corrected for the equilibration time [21].

All cardiocirculatory and respiratory data were collected as median values of 2 min from a patient data management system

Table 3 Regional hemodynamics

	Splanchnic Hemodynamics and Metabolism		
	Baseline	Increased PEEP	Baseline
Bloodflow (l/min/m^2)	0.91 (1.39–0.62)	1.04 (1.75–0.54)	1.07 (1.42–0.68)
$P_{gastric\ mucosal}\ CO_2$–$P_{arterial}\ CO_2$ kPa	2.3 (12.8–2.0)	2.0 (14.5–1.4)	2.2 (8.8–1.4)
$P_{hepatic\ venous}\ CO_2$–$P_{arterial}\ CO_2$ kPa	0.6 (1.1–0.4)	0.5 (1.1–0.4)	0.5 (1–0.3)
Hepatic venous lactate/pyruvate	9.7 (10.6–5.7)	9.7 (14.2–6.4)	8.4 (12.4–7.3)
Lactate extraction %	39 (67–15)	42 (62–25)	39 (61–21)
Lactate uptake mmol/min/m^2	0.5 (1.1–0.3)	0.4 (1.0–0.3)	0.5 (0.9–0.3)
ICG-extraction %	58 (68–22)	55 (70–31)	48 (66–36)
Oxygen extraction %	40 (63–25)	41 (65–28)	35 (61–28)
Oxygen consumption ml/min/m^2	52 (77–39)	63 (84–41)	53 (72–47)
Hepatic venous pressure mm Hg	9.7 (21.0–5.6)	10.7 (21.0–5.8)[a]	10.0 (19.8–5.3)[b]
Hepatic venous occlusion pressure mm Hg	11.7 (27.0–6.8)	12.7 (26.0–10.4)	11.9 (22.0–8.3)
Hepatic venous – central venous pressure mm Hg	2.8 (10.0–0.7)	2.2 (9.9–0.1)	2.9 (9.5–0.6)
Hepatic venous occlusion – hepatic venous pressure mm Hg	2.0 (7.1–0.3)	2.1 (7.3–0.0)	2.3 (6.1–0.1)
Hepatic venous occlusion – central venous pressure mm Hg	5.4 (16.0–1.7)	5.5 (14.7–1.2)	6.0 (11.7–2.0)

* $P < 0.05$ vs baseline

(Clinisoft, Datex-Engstrom, Kuopio, Finland).The inspiratory and expiratory flow was measured by a heated pneumotachograph (3700 Hans Rudolph, Kansas City, Mo., USA) and the airway pressures by differential pressure transducers (Validyne MP 45; Validyne, Northridge, Calif., USA). All these parameters were recorded at 100 Hz (Direc, Raytech Instruments, Vancouver, Canada).

The static compliance of the respiratory system ($C_{ST,rs}$) and the static inspiratory ($P_{ST,i}$) and expiratory pressures ($PEEP_{tot}$) were measured using the airway occlusion technique [29] as $C_{ST,rs} = V_t/(P_{ST,i}–PEEP_{tot})$.

The baseline PEEP level was selected by the physician in charge according to the method described by Valta et al. [30, 31] in daily routine. The baseline PEEP and the tidal volumes were selected so that all patients were ventilated within the linear part of the pressure volume-curve. Using this method we could also determine the changes in end-expiratory lung volume after the onset of PEEP.

Statistical analysis

The differences between the measurements were analyzed by a Friedman-test and facultatively by a Student-Newman-Keuls test. The nonparametric test was used because of the small sample. Statistical significance was considered at $P < 0.05$. All results are presented as median/range.

Results

Increasing the pre-set PEEP by 5 cmH_2O resulted in an increase in total PEEP of 3–5 cmH_2O and in absolute values of total PEEP from 10 to 14 cmH_2O. The static compliance decreased in three patients and increased in three patients (Table 1).

Systemic hemodynamics and gas exchange (Table 2)

PEEP induced inconsistent changes in hemodynamics. Only central venous pressure increased significantly ($P < 0.05$). Changes in DO_2 were also inconsistent. The VO_2 and VCO_2 were stable.

Splanchnic hemodynamics and metabolism (Table 3)

PEEP induced no consistent changes in splanchnic blood flow. Variable individual changes were observed (Fig. 1) and these changes were neither related to changes in the static compliance nor to changes in cardiac index (Fig. 4). At the baseline, the gradient between the gastric mucosal and arterial PCO_2 was high in three patients, and the gradient between the hepatic venous and arterial PCO_2 was only moderately elevated in two patients. No consistent increases were observed in these gradients in response to PEEP (Fig. 2).The splanchnic VO_2 and oxygen extraction also remained stable. The hepatosplanchnic redox state as indicated by the lactate/pyruvate ratio remained constant as well. The indocyanine green extraction, a marker of liver function, did not change significantly either.

The increase in PEEP induced a small but significant increase in HVP and inconsistent changes in HVOP (Table 3). The changes in driving pressures of venous return were very small, except in one patient, and not related to changes in splanchnic blood flow (Fig. 3).

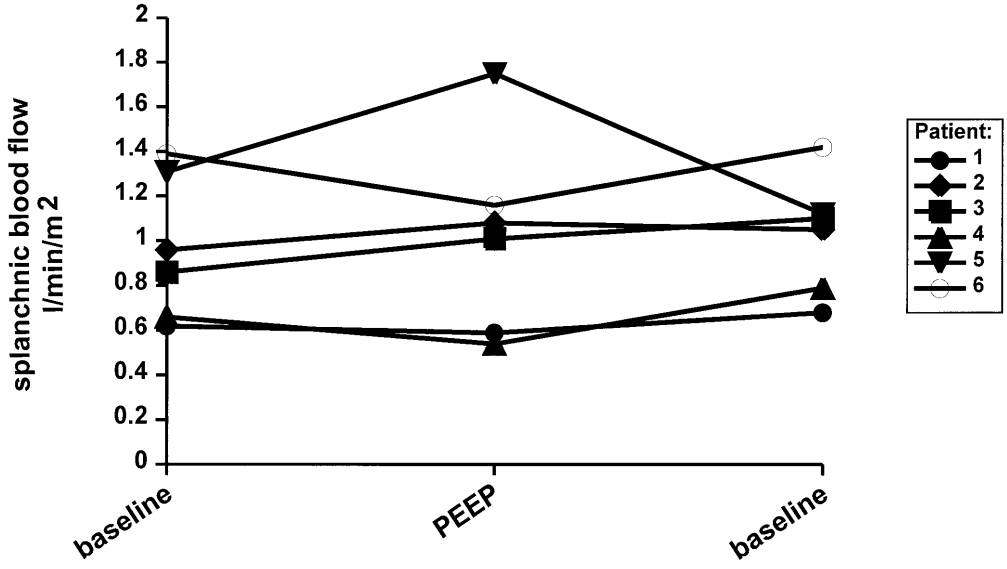


Fig. 1 Individual changes in splanchnic blood flow after an increase and decrease in PEEP

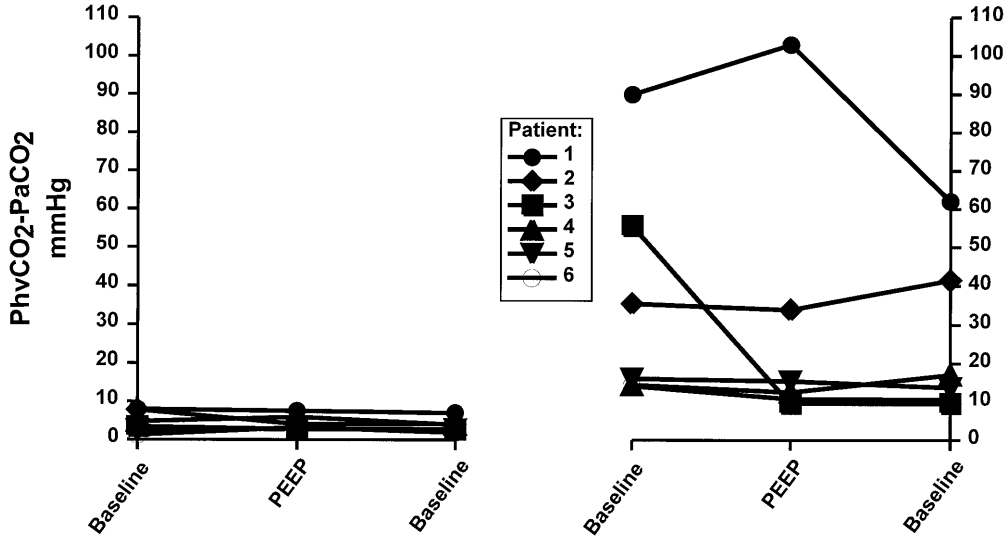


Fig. 2 Individual changes in $PhvCO_2$-$PaCO_2$ and $PgmCO_2$-$PaCO_2$gradients under the influence of PEEP (*$PhvCO_2$* hepatic venous carbon dioxide partial pressure, *$PaCO_2$* arterial carbon dioxide partial pressure, *$PgmCO_2$* gastric mucosal carbon dioxide partial pressure

Discussion

This is the first study on the effects of PEEP on splanchnic tissue perfusion in patients with severe acute lung injury. The main findings were that first, PEEP did not have consistent effects on splanchnic tissue perfusion, as assessed by total hepatosplanchnic blood flow, gastric mucosal tonometry, and regional CO_2-gradients. Second, PEEP had no effect on indices of hepatosplanchnic metabolism and liver function, as indicated by the hepatosplanchnic lactate to pyruvate ratio, lactate extraction and uptake, and indocyanine green extraction. This was the case even if signs of marginal splanchnic tissue perfusion, such as increased PCO_2 gradients, were present before the increase in PEEP. The findings should be considered in the context of practically unchanged systemic hemodynamics.

Measurement of hepatosplanchnic blood flow by dye-dilution is the basis of our results and their interpretation. Previous experimental studies have suggested that the intrahepatic handling of indocyanine green is altered by PEEP [10, 12]. If the hepatosplanchnic blood flow were measured by bolus injection of indocyanine green, this would form a major problem. The cited previous experimental studies used back-extrapolation of indocyanine green concentration to estimate the steady state indocyanine green extraction instead of measuring the steady state indocyanine green extraction. If the hepatic handling of the dye is altered, as has been suggested, the results will not be valid. In contrast, we mea-

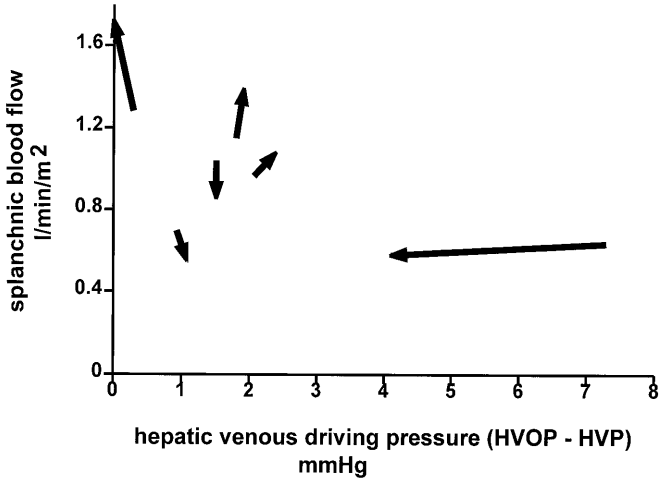
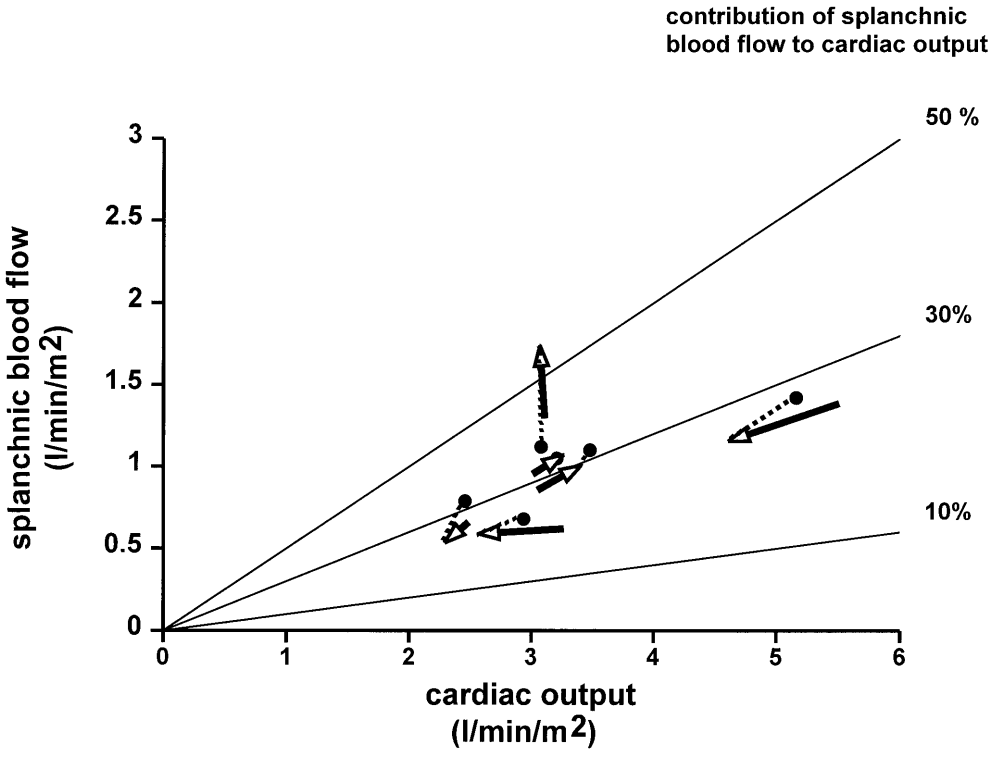


Fig. 3 Individual changes in splanchnic blood flow and hepatic venous occlusion pressure-hepatic venous pressure gradients (HVOP-HVP) and their correlation after an increase in PEEP

sured the steady state extraction of the dye, and hence, the blood flow estimation remains valid despite any possible changes in intra-hepatic dye handling. The only mechanisms theoretically interfering with our method, would be induction of an extra-hepatic dye elimination by application of PEEP. This has never been demonstrated. Accordingly, methodological problems are unlikely to explain our observations.

The main weakness of our study is the small sample size. The lack of consistent changes of relevant magnitude or patterns of changes in the different independent measures of splanchnic perfusion and function makes it unlikely that increasing the sample size would have altered the results. Most previous studies reporting reduced splanchnic blood flow in response to PEEP have observed consistent and marked flow changes in small series [10, 11, 12, 13, 14, 18, 19, 20]. Failure to detect changes in splanchnic blood flow should be considered as a potential explanation for the lack of consistent changes in blood flow in the present study. We have previously demonstrated that the splanchnic blood flow can be measured in various groups of intensive care patients, including patients with severe acute lung injury, with good reproducibility [24]. In this study, the dye extraction was adequate and the coefficient of variation for the repeated blood flow measurements was small. Furthermore, we used several mutually independent markers of different aspects of splanchnic perfusion: the hepatic venous-arterial PCO_2 gradient as another index of total hepatosplanchnic perfusion, the mucosal-arterial PCO_2 gradient as a marker of local perfusion and the hepatic venous lactate to pyruvate ratio as an index of the hepatosplanchnic redox-state; none of these showed any change in response to PEEP. In addition, the functional and metabolic markers, i.e., hepatosplanchnic oxygen uptake and extraction, lactate extraction and uptake, and indocyanine green extraction, also

Fig. 4 Individual changes in splanchnic blood flow and cardiac index after changes in PEEP (*solid arrow*: increase in PEEP, *dashed line*: reduction of PEEP back to baseline)



remained stable, further indicating the lack of PEEP-induced changes. Nevertheless, we observed in individual patients changes in cardiac output and splanchnic blood flow that may be clinically relevant. It is possible that a substantially larger sample of patients might allow us to identify subgroups of patients, where predictable regional hemodynamic responses to PEEP could be observed.

Several experimental studies [10, 11, 12, 13] have reported marked and consistent reductions in total splanchnic and portal venous blood flow in response to PEEP. These changes have accompanied similar reductions in cardiac output. Also, in patients undergoing laparotomy [18, 20] or after polytrauma [19], PEEP reduced portal venous flow in parallel with decreases in cardiac output. In contrast, Matuschack et al. [12] and Brienza et al. [11] demonstrated that the PEEP-induced reduction in portal and total hepatic blood flow were normalized after normalizing the cardiac output by infusion of fluids. The main difference between our study and most of the studies in the literature [10, 11, 12, 13, 14, 18, 19, 32] is that we observed no consistent changes in cardiac output in response to PEEP (Fig. 2). We suggest that the lack of major changes in cardiac output in our patients was related to adequate fluid management with enhanced venous return prior to increasing the PEEP. In some of the previous reports, volume management has either not been specified [10, 11], or the intravascular filling pressures have been low [12]. Accordingly, relative hypovolemia is likely to have contributed to the previously observed reductions in cardiac output and splanchnic blood flow.

A major influence on our results may have been that the initial PEEP was selected according to the pv-curve. All patients were ventilated in the linear part of the pv-curve, avoiding high tidal volumes and inspiratory pressures. After the increase in PEEP the tidal volumes and the ventilatory pressures were still in the curve-linear part of the pv-curve.

The increase in intrathoracic pressure by PEEP resulted in an increase in intrathoracic vascular pressures (Table 3) and intraabdominal vascular pressures (Table 2). The driving pressures of venous return (Table 2) were constant, probably due to an adequate filling volume. It has been shown that at adequate filling volume the application of PEEP may even improve left ventricular function [9] which is reflected in our study by the well-maintained stroke volume index [baseline: 33 (49–28) ml/str.; PEEP: 35 (45–28) ml/str.] and thereby contribute to the stable cardiac index and splanchnic blood flow.

Another mechanism of PEEP influencing the splanchnic blood flow is described by Brienza et al. [33]. In a septic liver model the authors showed that at adequate filling volume the decrease in liver blood flow is mainly determined by direct compression of the liver by diaphragmatic descent.

In our patients the increase in PEEP resulted in an increased endtidal volume of 298 ml (median; range 140–437 ml). This volume could be seen as the maximum volume that could alter intraabdominal pressure.

Since the driving pressures of venous return were kept constant (Table 2) it is likely that the intraabdominal compliance in our patients was not reduced. This may have caused an equal distribution of increased volume between the thorax and the abdomen. Another suitable reason for the unchanged cardiac index and splanchnic blood flow might be, that in the presence of an intact hepatic waterfall [34] splanchnic blood flow is not altered by increased hepatic venous pressure. The principle of the hepatic waterfall was first described by Mitzner et al. [34] who showed that up to a certain level of increased HVP neither the sinusoid pressure nor the liver blood flow were altered. Even a negative HVP could not increase the liver blood flow. The authors therefore assumed that the blood flow across the liver is similar to a waterfall. The hepatic waterfall buffering the elevated hydrostatic backpressure together with the other mechanisms described above may have counterbalanced each other resulting in small, inconsistent changes in splanchnic blood flow.

The effects of PEEP on the splanchnic perfusion and metabolic functions may be time-related. Since we observed the responses over a period of 90 min only, we cannot exclude long-term changes. Nevertheless our observation period was longer than in most of the previous studies, and transient changes occuring acutely after application of PEEP might explain some of the differences between our results and previous studies.

Our results, in agreement with the experimental studies of Matuschack [12] and Brienza [11, 33], strongly suggest that changes in PEEP do not influence splanchnic perfusion, unless accompanied by changes in cardiac output. We emphasize that this was observed within a relatively narrow but clinically relevant range of PEEP in patients who were hemodynamically stable without the use of adrenergic agents. Selecting the PEEP and the tidal volume in a range such that the patient is ventilated in the steep part of the pressure volume curve, might keep cardiac index and splanchnic blood flow constant. From the clinical point of view, maintenance of cardiac output during changes in PEEP should prevent potential impairment of splanchnic perfusion.

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