Intensive Care Med (1996) 22:772–780

ORIGINAL

M. Dambrosio
G. Fiore
N. Brienza
G. Cinnella
M. Marucci
V.M. Ranieri
M. Greco
A. Brienza

Right ventricular myocardial function in ARF patients

PEEP as a challenge for the right heart

Received: 29 December 1994
Accepted: 11 April 1996

Partially supported by Consiglio Nazionale delle Ricerche grant, Italy

M. Dambrosio (✉) · G. Fiore
N. Brienza · G. Cinnella · M. Marucci
V.M. Ranieri · M. Greco · A. Brienza
Istituto di Anestesiologia e Rianimazione,
Università degli Studi di Bari, Policlinico,
Piazza Giulio Cesare, 70124 Bari, Italy;
FAX: +39(80)5478756;
Tel.: +39(80)5473532/3535;
e-mail: rianima@cimedoc.uniba.it

Abstract *Objective:* To examine the hemodynamic effects of external positive end-expiratory pressure (PEEP) on right ventricular (RV) function in acute respiratory failure (ARF) patients.
Design: Prospective, with retrospective analysis on the basis of RV volume response to PEEP.
Setting: General intensive care unit in a university teaching hospital.
Patients: 20 mechanically ventilated ARF patients (mean lung injury score = 2.6±0.45 SD).
Intervention: Incremental levels of PEEP (0–5–10–15 cmH_2O) were applied and RV hemodynamics were studied by means of a Swan-Ganz catheter with a fast-response thermistor for right ventricular ejection fraction (RVEF) measurement. According to their response to PEEP 15, two groups of patients were defined: group A (9 patients) with unchanged or increased RV end-diastolic volume index (RVEDVI) and group B (11 patients) with decreased RVEDVI.
Measurements and results: At zero PEEP (ZEEP) the hemodynamic parameters of the two groups did not differ. In group A, cardiac index (CI) and stroke volume index (SI) decreased at all PEEP levels (5, 10, and 15 cmH_2O), while RVEF started to decrease only at a PEEP of 10 cmH_2O (−10.8%), and RVES(systolic)VI increased only at PEEP 15 cmH_2O (+21.5%). RVEDVI was not affected by PEEP. In group B, CI and SI decreased at all PEEP levels (5, 10, and 15 cmH_2O). Similarly, RVEDVI started to decrease at PEEP 5 cmH_2O, while RVESVI decreased only at PEEP 15 cmH_2O (−21.4%). RVEF was not affected by PEEP in this group. In each patient the slope of the relationship between RVEDVI and right ventricular stroke work index (RVSWI), expressing RV myocardial performance, was studied. This relationship was significant (no change in RV contractility) in 8 of 11 patients in group B and in only 2 patients in group A. In 4 patients in group A, PEEP shifted the RVSWI/RVEDVI ratio rightward in the plot, indicating a decrease in RV myocardial performance in these patients.
Conclusions: PEEP affects RV function in ARF patients. The decrease in cardiac output is more often associated with a preload decrease and no change in RV contractility. On the other hand, the finding of increased RV volumes with PEEP may be associated with a reduction in RV myocardial performance. Thus, these results suggest that assessment of RV function by PEEP and preload recruitable stroke work may disclose otherwise unpredictable alterations in RV function.

Key words ARF PEEP · PRSW RVEDVI RVEF Right ventricular function

Introduction

Positive end-expiratory pressure (PEEP), usually used to improve pulmonary oxygen exchange in acute respiratory failure (ARF), causes a reduction in cardiac output (CO) [1]. This has been mainly related to a reduction in venous return [2, 3]. Furthermore, an increased alveolar volume can exert a Starling resistor effect on the pulmonary circulation, thus increasing pulmonary pressure load on right ventricular (RV) ejection [4, 5].

The reduction in CO, related to an increased RV afterload, is often associated with an increase in RV volumes [6–9]. Such RV dilation could be due to: (a) the preload reserve utilization according to the Frank–Starling law; (b) a change in ventricular geometry, causing alteration of the ejection pattern [10]; (c) decreased contractility [8, 9] due to a mismatch between increased RV work and decreased RV perfusion [11]. In postoperative patients, RV contractility has been evaluated by the systolic pressure–volume relationship (simplified maximal elastance or Emax-ti) [8], but this measurement has been considered weak for evaluating RV contractility [12]. Moreover, the maximal elastance model (Emax) has often been criticized because of its low reproducibility [13, 14]. Recently, it has been proposed that the relationship between ventricular stroke work and end diastolic ventricular volume at different preload levels evaluates ventricular performance [13]. This relationship, i.e., preload recruitable stroke work (PRSW), has been considered easier to perform and more easily reproducible than the Emax model [13–15] and has also been validated for RV function [16].

The aim of this study was to investigate RV myocardial performance in ARF patients, evaluated by the PRSW model, using different PEEP levels in order to change RV preload and afterload.

Materials and methods

Patients

Twenty patients with ARF, admitted to the intensive care unit (ICU) of the University Hospital in Bari, were studied. The study protocol was approved by the local Ethics Committee and each patient or next of kin gave informed consent. The lung injury score (LIS) [17] was computed in all patients admitted to the ICU and a LIS ≥ 2 was required for inclusion in the study. Patients with pre-existing cardiac or pulmonary disease were not included in the study. All patients (11 males, 9 females; mean $\pm$ SD age, 51 ± 15 years) were intubated and mechanically ventilated (Servo Ventilator 900C Siemens Elema AB, Berling, Germany) with a tidal volume level (10 ± 2 ml/kg) in order to maintain normal partial pressure of carbon dioxide in arterial blood, with a respiratory rate of 18 breaths/min, and with an inspiration/expiration ratio of 1 : 2. The patients were ventilated for a mean($\pm$SD) period of 12 (± 14) days (ranging from 7 to 72 days). The etiologies of ARF are shown in Table 1.

Experimental procedures

The ventilatory setting was kept constant throughout the procedure, except for the level of PEEP. PEEP levels of 0, 5, 10, and 15 cmH_2O were applied in random order for 30 minutes before measurements were made. A physician not involved in the experimental procedure was always present to provide patient care, and use of fluids and therapy was not changed during the study phase.

A 20-gauge radial arterial catheter (Arrow International, Reading, Penna., USA, Model RA-04020-E) was inserted percutaneously to measure systemic arterial pressure. A pulmonary arterial Swan-Ganz catheter with a fast-response thermistor (Baxter-Edwards, Irvine, Calif., USA, Model 93A-431H 7.5 F) was inserted into the pul-

Table 1 Patients (*LIS* lung injury score, *S* survived, *D* died)

Patient no.	Age (years)	Weight (kg)	Sex	Precipitating causes of ARF	LIS	Outcome
1	28	72	M	Multiple trauma	2.7	S
2	46	80	M	Pancreatitis	3.3	S
3	58	68	F	Bronchopneumonia in tetanus	2.0	S
4	38	67	M	Multiple trauma	2.3	D
5	76	71	F	Sepsis in peritonitis	2.0	D
6	66	52	M	Postoperative bronchopneumonia	2.0	S
7	66	46	F	Sepsis in perforation of gastric ulcer	2.3	D
8	62	57	F	Sepsis in colectomy	3.0	S
9	47	91	M	Pancreatitis	2.7	D
10	40	58	F	Sepsis in gut ischemia	2.7	S
11	61	63	F	Pancreatitis	3.3	D
12	25	48	F	Sepsis in leukemia	3.3	D
13	69	65	M	Sepsis in endocarditis	2.7	D
14	60	68	M	Multiple trauma	2.5	S
15	32	84	M	Multiple trauma and fat embolism	2.7	D
16	46	59	F	Sepsis in peritonitis	2.0	D
17	28	63	M	Multiple trauma	3.3	S
18	47	74	M	Sepsis in mediastinitis	3.0	D
19	48	91	M	Viral pneumonia	2.2	D
20	69	67	F	Sepsis in hysterectomy	2.7	D

monary artery to measure pulmonary arterial pressure (PAP), pulmonary arterial occlusion pressure (Ppao), and right atrial pressure. The positioning of the catheter tip in the pulmonary artery was guided by the wave morphology during the introduction. The positioning in the segment of lung reflecting Zone 3 condition was obtained using the method described by Teboul et al. [18]. In order to measure correctly both CO and RV ejection fraction (RVEF), the position of the hole for injection was 2 cm above the tricuspid valve [19].

Measurements

The patients were sedated (diazepam 0.2 mg/kg and fentanyl 1–1.5 μg/kg per h) and paralyzed (vecuronium bromide 0.1 mg/kg per h) and 30 min were allowed in order to achieve hemodynamic stabilization. The arterial and pulmonary arterial catheters were connected to pressure quartz transducers (Hewlett-Packard P1290A Cupertineo, Calif., USA). The midaxillary line was taken as zero reference level for pressure measurements, with the patient supine and horizontal, and all pressures were read at end-expiration. All signals were recorded with an eight-channel strip chart recorder (Hewlett-Packard 7719A). CO was measured by the thermodilution technique (Edwards-Baxter REF-1 Ejection Fraction/Cardiac Output Computer) using injections of 5 ml cold (<5 °C) 5% dextrose solution. Seven serial determinations were made, regardless of the respiratory cycle phases [20]. If any CO determination during each step of PEEP varied more than 10%, or arrhythmias occurred during the recording, the measurement was rejected. RVEF was calculated from the analysis of the thermal curve both by validated software [21] of the CO computer (Edwards-Baxter REF-1) and by calculation of the difference among several consecutive plateaux of the thermal decay curve [19]. The RVEF measurement was rejected if the difference between automatic and manual calculation was greater than 2.5% or if an abnormal curve profile was detected. During PEEP, none of the patients had tricuspid regurgitation, as shown both by the analysis of right atrial pressure wave morphology and by physical examination. None of the 5 patients (3 with PEEP-induced RVEDVI increase) who underwent a B-mode echocardiographic evaluation showed a regurgitation higher than 13% [22].

Cardiac index (CI) was computed as the ratio between CO and body surface area. Stroke volume index (SI) was calculated by dividing CI by heart rate (HR). Right ventricular stroke work index (RVSWI) ($g \cdot min/beat \cdot m^2$) was calculated as the pressure gradient between mean pulmonary arterial pressure (mPAP) and right atrial pressure (RAP), multiplied by SI:

$$RVSWI = (mPAP - RAP) \times SI$$

Right ventricular end-diastolic volume index (RVEDVI) and right ventricular end-systolic volume index (RVESVI) were calculated by the following formulae:

$$RVEDVI = SI/RVEF$$

$$RVESVI = RVEDVI - SI$$

Right ventricular intrinsic myocardial performance was considered in each patient as the slope of the RVSWI versus RVEDVI relationship [13–16] obtained by fitting data at four PEEP levels by the least-squares linear regression analysis.

In order to distinguish the preload effect by other PEEP effects, the total sample was divided in two groups on the basis of the RVEDVI response to PEEP 15 cmH_2O: patients with an increased, unchanged, or decreased RVEDVI less than 10% of zero PEEP (ZEEP) value (group A), and patients with an RVEDVI decreased more than 10% of ZEEP value (group B).

Data analysis

All data are reported for descriptive statistics as mean ± SD. Regression analyses were performed with the least-squares method. A one-way analysis of variance (ANOVA) was used to compare values obtained at different levels of PEEP. When significant, the values obtained at different levels of PEEP were compared with those at ZEEP, using the paired *t*-test as modified by Dunnet [23]. At ZEEP, hemodynamic data for groups A and B were compared by the unpaired *t*-test. A value of $p < 0.05$ was considered to be significant.

Results

Table 1 shows each patient's age, weight, sex, precipitating cause of ARF, LIS, and outcome. The effects of PEEP on the hemodynamics of the whole group of patients are shown in Table 2. At PEEP 5 cmH_2O, there was a significant decrease in CI (−7.6%) and SI (−5.7%). These two parameters were further reduced at PEEP 10 and 15 cmH_2O. No change in HR, RVEF, RVEDVI, and RVESVI was observed. PEEP increased the mean oxygen arterial saturation.

In group A, 9 patients (5 with increased RVEDVI and 4 with unchanged RVEDVI at PEEP 15) were included. In group B, 11 patients (more than 10% decrease in RVEDVI) were included. At ZEEP, there was no significant difference in CI, HR, SI, RVEF, RVEDVI, and RVESVI between groups A and B.

Table 3 shows the mean hemodynamic and gas exchange data for group A. Mean hemoglobin value was 9.7 ± 0.4 g/dl, and it was constant at all PEEP levels. The

Table 2 Effects of PEEP on hemodynamics in all patients ($n = 20$). Values are mean ± SD (*HR* heart rate, *CI* cardiac index, *SI* stroke volume index, *RVEF* right ventricular ejection fraction, *RVEDVI* right ventricular end-diastolic volume index, *RVESVI* right ventricular end-systolic volume index

	PEEP 0	PEEP 5	PEEP 10	PEEP 15	ANOVA
HR (beats/min)	102.2 ± 17.1	100.1 ± 16.6	100.1 ± 16.2	100.6 ± 17.8	NS
CI (l/m^2)	4.62 ± 1.2	4.27 ± 1.1****	4.09 ± 0.9****	3.74 ± 0.8****	###
SI (ml/m^2)	46.1 ± 11.9	43.5 ± 11.1****	41.9 ± 11.3***	38.5 ± 11.2****	###
RVEF (%)	43.5 ± 6.4	42.4 ± 6.7	41.2 ± 6.3	40.6 ± 6.9	NS
RVEDVI (ml/m^2)	107.3 ± 29.8	104.4 ± 28.7	104.1 ± 32.7	97.6 ± 33.9	NS
RVESVI (ml/m^2)	61.2 ± 21.6	61.9 ± 21.0	62.2 ± 23.9	59.2 ± 25.4	NS

#$p < 0.01$, ##$p < 0.001$, ###$p < 0.0001$ ANOVA
*$p < 0.05$, **$p < 0.025$, ***$p < 0.01$, ****$p < 0.005$ *t*-test as modified by Dunnet [23]

Table 3 Effects of PEEP on hemodynamics: group A ($n = 9$). Values are mean ± SD (*HR* heart rate, *CI* cardiac index, *SI* stroke volume index, *RVEF* right ventricular ejection fraction, *RVEDVI* right ventricular end-diastolic volume index, *RVESVI* right ventricular end-systolic volume index, *RAP* right atrial pressure, *mPAS* mean systemic blood pressures, *sPAP, dPAP, mPAP* systolic, diastolic, and mean pulmonary arterial pressure, *Paop* pulmonary artery occlusion pressure, *RVSWI* right ventricular stroke work index, SvO_2 mixed venous oxygen saturation)

	PEEP 0	PEEP 5	PEEP 10	PEEP 15	ANOVA
HR (beats/min)	99.8 ± 21.1	96.3 ± 18.9	96.1 ± 19.7	94.2 ± 2.2	NS
CI (l/m^2)	4.43 ± 1.1	4.04 ± 1.1*	4.0 ± 1.0***	3.76 ± 1.0****	###
SI (ml/m^2)	46.26 ± 14.4	43.40 ± 13.7*	43.21 ± 13.8**	41.74 ± 13.4**	##
RVEF (%)	44.5 ± 4.8	41.6 ± 4.6	39.7 ± 4.1****	37.97 ± 4.5****	##
RVEDVI (ml/m^2)	103.69 ± 32.6	104.13 ± 29.7	109.96 ± 38.5	111.31 ± 40.1	NS
RVESVI (ml/m^2)	57.36 ± 19.7	60.75 ± 17.1	66.80 ± 25.9	69.68 ± 28.1***	#
RAP (mmHg)	7.77 ± 4.5	9.61 ± 4.7**	9.61 ± 4.4***	11.05 ± 4.1***	###
mPAS (mmHg)	90.42 ± 17.7	90.87 ± 20.1	91.96 ± 17.0	89.59 ± 19.9	NS
sPAP (mmHg)	31.66 ± 7.7	32.20 ± 6.9	32.66 ± 6.4	33.88 ± 6.9	NS
dPAP (mmHg)	16.66 ± 4.3	18 ± 4.1	18.88 ± 3.8	20.61 ± 3.4**	##
mPAP (mmHg)	21.55 ± 4.8	22.61 ± 4.4	24.20 ± 4.5	25.70 ± 4.6*	##
Ppao (mmHg)	10.84 ± 4.7	12.72 ± 4.8*	12.27 ± 4.3	14 ± 4.2***	###
RVSWI (g min/beat m^2)	8.86 ± 3.1	7.85 ± 3.2	8.68 ± 2.8	8.30 ± 2.7	NS
pH	7.47 ± 0.07	7.47 ± 0.07	7.46 ± 0.07	7.47 ± 0.07	NS
PaO_2 (mmHg)	90 ± 16	102 ± 25	112 ± 36*	115 ± 33*	##
$PaCO_2$ (mmHg)	37 ± 8	36 ± 7	38 ± 8	38 ± 7	NS
SvO_2 (%)	72 ± 4	71 ± 4	72 ± 4	72 ± 4	NS

#$p<0.01$, ##$p<0.001$, ###$p<0.0001$ ANOVA
*$p<0.05$, **$p<0.025$, ***$p<0.01$, ****$p<0.005$ *t*-test as modified by Dunnet [23]

mean value of RVEDVI did not change significantly with PEEP. CI (−8.8%) and SI (−6.7%) decreased at PEEP 5 cmH_2O and were further reduced at PEEP 10 and 15 cmH_2O, confirming the data for in the whole group. RVEF started to decrease at PEEP 10 cmH_2O (−10.8%), and RVESVI increased only at PEEP 15 cmH_2O (+21.5%). RAP, Ppao, and mPAP all increased with PEEP.

Mean hemodynamic and gas exchange data for group B are presented in Table 4. Mean hemoglobin value was 10.1 ± 1.2 g/dl, and it was constant at all PEEP levels. Mean RVEDVI decreased at PEEP 5 cmH_2O (−5.2%), and further decreased with higher PEEP levels. CI (−6.5%), SI (−6.2%) and RVSWI (−12.2%) were reduced by 5 cmH_2O of PEEP and further decreased at PEEP 10 and 15 cmH_2O. RVEF did not change, and

Table 4 Effects of PEEP on hemodynamics. Group B ($n = 11$). Values are mean ± SD (Definitions as in Table 3)

	PEEP 0	PEEP 5	PEEP 10	PEEP 15	ANOVA
HR (beats/min)	104 ± 13.6	103 ± 14.6	103.3 ± 12.5	105.8 ± 11.9	NS
CI (l/m^2)	4.77 ± 1.2	4.46 ± 1.1*	4.17 ± 0.9*	3.73 ± 0.7****	###
SI (ml/m^2)	45.94 ± 10.1	43.54 ± 9.1*	40.84 ± 9.3	35.91 ± 8.8****	###
RVEF (%)	42.6 ± 7.6	42.9 ± 8.2	42.4 ± 7.7	42.7 ± 8.0	NS
RVEDVI (ml/m^2)	110.2 ± 28.5	104.5 ± 29.2**	99.3 ± 28.2	86.4 ± 24.3****	###
RVESVI (ml/m^2)	64.3 ± 23.4	61.0 ± 24.5	58.4 ± 22.6	50.5 ± 20.3****	#
RAP (mmHg)	8.76 ± 2.1	9.97 ± 3.3	11.31 ± 2.1***	12.86 ± 2.4****	###
mPAS (mmHg)	94.4 ± 15.7	95.9 ± 19.4	95.3 ± 20.3	95.6 ± 20.1	NS
sPAP (mmHg)	35.3 ± 7.0	34.2 ± 7.4	36.3 ± 6.4	38.4 ± 6.1*	#
dPAP (mmHg)	20.0 ± 3.7	20.8 ± 4.1	22.0 ± 4.4	24.5 ± 3.6****	###
mPAP (mmHg)	25.3 ± 4.2	25.2 ± 4.9	26.9 ± 4.5	29.3 ± 3.6****	###
Ppao (mmHg)	12.9 ± 4.4	13.0 ± 4.9	14.4 ± 4.1	16.9 ± 3.9****	###
RVSWI (g min/beat m^2)	10.79 ± 3.2	9.47 ± 3.3**	9.15 ± 3.1	8.49 ± 2.9**	#
pH	7.50 ± 0.08	7.50 ± 0.09	7.50 ± 0.08	7.50 ± 0.07	NS
PaO_2 (mmHg)	87 ± 49	104 ± 44*	122 ± 61	148 ± 76*	##
$PaCO_2$ (mmHg)	38 ± 8	36 ± 8	35 ± 8	36 ± 7	NS
SvO_2 (%)	73 ± 5	74 ± 6	74 ± 5	73 ± 4	NS

#$p<0.01$, ##$p<0.001$, ###$p<0.0001$ ANOVA
*$p<0.05$, **$p<0.025$, ***$p<0.01$, ****$p<0.005$ *t*-test as modified by Dunnet [23]

RVESVI decreased only at PEEP 15 cmH_2O (−21.4%). RAP, Ppao, and mPAP all increased with PEEP.

In each patient a linear regression analysis between CI and RVEDVI was performed. Taking into account all four levels of PEEP, no relationship was found in the 9 patients in group A (Fig. 1, top), while a significant relationship between CI and RVEDVI was found in 10 of the 11 patients in group B (Fig. 1, bottom).

Linear regression analyses between RVESVI and mPAP were also performed. Five patients in group A (patients 1–5) showed a significant direct relationship between RVESVI and mPAP ($r = 0.95$, 0.87, 0.89, 0.90, and 0.99 for patients 1, 2, 3, 4, and 5, respectively), while this relationship was not significant in any patient in group B.

Linear regression analyses performed between RVSWI and RVEDVI were significant in only 2 of 9 patients in group A (patients 5 and 6) (Fig. 2, top) and in 8 of 11 patients in group B (Fig. 2, bottom). More specifically, examining the behaviour of each patient in group A, a scattered distribution of the RVSWI/RVEDVI plot was observed in 3 patients, while a rightward shift of the RVSWI/RVEDVI plot was observed in 4 patients (1, 3, 4, 9).

Discussion

In the present study, PEEP caused a decrease in CO. This reduction can be ascribed to two different mechanisms. On the one hand, the reduction in CO is due to a preload decrease (group B), as evidenced by the reduction in right ventricular end-diastolic volume and by the significant relationship between CI and RVEDVI. In these patients, the preload reduction was associated with unchanged RV contractility, as shown by the presence of a significant relationship between RVSWI and RVEDVI. On the other hand, PEEP can reduce CO by a predominant afterload effect (group A), as evidenced by the increase in right ventricular end-systolic volume and by the decrease in RVEF. The afterload effect during PEEP may cause a reduction in RV contractility, as evidenced by the rightward shift of RVSWI/RVEDVI plot in 4 patients.

Critique of the methods

In the present study, RV preload was estimated as right ventricular end-diastolic volume, rather than transmural filling pressure. Positive end-expiratory ventilation either decreases [24] or does not change [10] transmural filling pressures. These conflicting results seem strictly dependent on the position of the thoracic probe (used to measure the intrathoracic and/or pericardial pressures) and on the type and material of transducers. In decompensated and ventilated patients with chronic obstructive pulmonary disease [25], Dambrosio et al. observed that the decrease in RVEDVI caused by PEEP was significantly related to end-expiratory lung volume variations, rather than to transmural pressure changes. Thus, ventricular

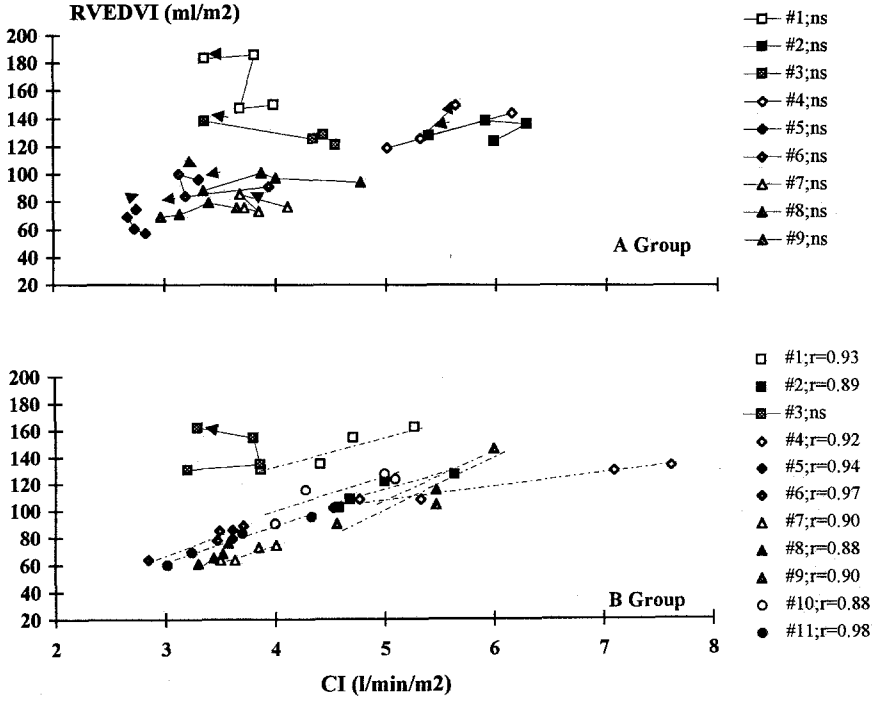


Fig. 1 For each patient in groups A and B, the relationships between right ventricular end-diastolic index *RVEDVI* and cardiac index *CI* are shown. Each point refers to a single PEEP level. The arrows point to PEEP 15. Significant relationships are indicated by dotted lines

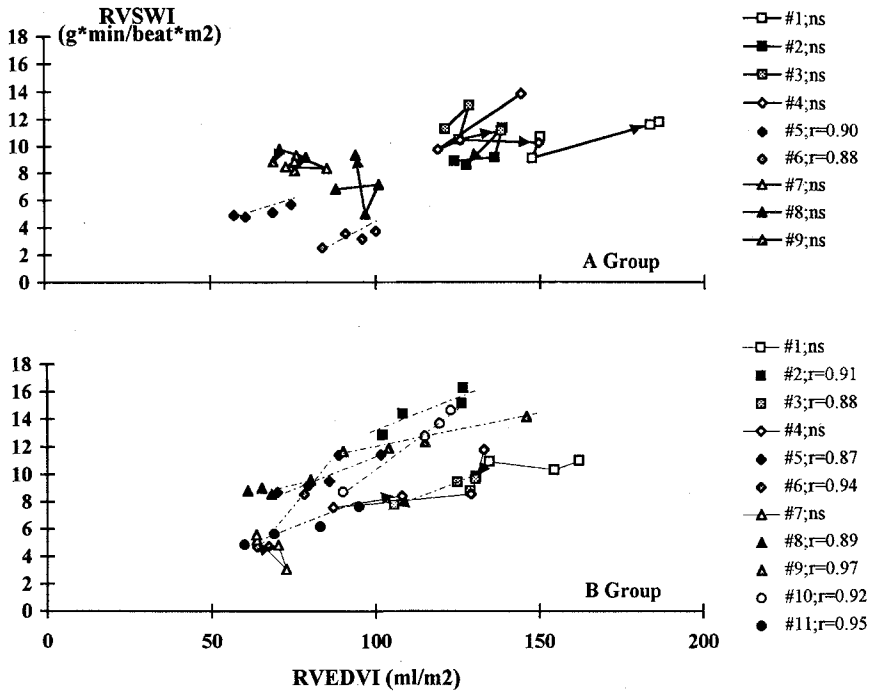


Fig. 2 For each patient in groups A and B, the relationships between right ventricular stroke work index *RVSWI* and right ventricular end-diastolic volume *RVEDVI* are shown. Each point refers to a single PEEP level. The arrows point to PEEP 15. Significant relationships are indicated by dotted lines

volumes are a more reliable index of right ventricular preload than transmural filling pressures [21, 26].

In the clinical setting, thermodilution is an easy, reproducible, and reliable technique to measure right ventricular volumes [21, 26]. However, RV valve regurgitation may invalidate the measurement of RV volumes by this technique [22], since it causes an overestimation of both CO and RV volumes. Moreover, regurgitation may increase with PEEP [12] and is more likely to occur in dilated ventricles. In the present study, analysis of the RAP wave morphology and physical examination excluded the presence of clinically significant regurgitation. Echocardiographic evaluation, performed in 5 patients (3 patients in group A), did not show a regurgitation more than 13% at all PEEP levels [22]. Furthermore, if PEEP had enhanced valve regurgitation, with the consequent CO overestimation, CO should not have decreased with PEEP. Moreover, if the ventricular dilation induced by PEEP had caused more regurgitation, it would have been highly unlikely to find a similar reduction in cardiac output in the two groups. In group A, only RV volumes increased with PEEP, while a weakness of the thermodilution technique induced by valve regurgitation should have shown variations of CO and ventricular volume in the same direction. The relationship between mPAP and RVESVI found in most patients in group A, indicating a PEEP afterload effect on RV, supports the hypothesis that the increase in RV volumes is related to PEEP. Thus, it is most likely that the results of the present study are related to a real PEEP effect, rather than to a weakness of the thermodilution method.

The finding of RV dilation during PEEP has led several authors to evaluate RV performance [8–10]. In order to investigate RV contractility with PEEP, the end-systolic pressure–volume relationship (Emax) has been simplified as the ratio between pulmonary artery systolic pressure and RV end-systolic volume [8, 9]. However, the application of this simplified Emax model to the right ventricle has been criticized because of the known lack of correspondence between end-systole and end-ejection in the right ventricle [12]. Moreover, recently it has been reported that Emax is not always linear [14]. In order better to evaluate ventricular performance, Glower et al. [13] have proposed the relationship between stroke work and end-diastolic volume, ie., the PRSW. This relationship has been proposed as a measure of intrinsic myocardial performance independent of loading, geometry, and HR [13]. The advantages of the PRSW are that this index is as reliable as Emax, easier to measure than Emax, is always linear, and is unaffected by pressure transmission [15]. The PRSW has been recently validated in both experimental [14] and clinical [15] settings, since the behavior of this index is similar to Emax. Karunanithi et al. [16] have proposed the relationship between RVSWI and RVEDVI specifically for the right ventricle, based on the experimental finding that PRSW is more accurate and reproducible, and less afterload-dependent than Emax. Clinical application of this index to the right ventricle has recently been reported [7, 27]. In order to obtain an accurate PRSW, a pure preload variation is necessary. As a matter of fact, PEEP reduces preload [2, 3]. Thus, if PEEP reduces RVEDVI without modifying RV contractil-

ity and afterload, then a linear relationship between RVSWI and RVEDVI should be found, expressing a constant PRSW and, hence, constant contractility.

Effects of PEEP on RV function

In 11 patients, the CO reduction induced by PEEP was associated with a preload reduction (group B), as evidenced by the decrease in RVEDVI. This effect is further confirmed by the individual relationships between CO and RVEDVI (Fig. 1, bottom). The presence of a significant relationship between RVSWI and RVEDVI expresses a constant function and suggests an unchanged contractility in these patients. This is an expected behavior in the presence of a predominant preload effect.

In 9 patients, the CO reduction with PEEP was associated with no decrease in RVEDVI. However, RVESVI increased and RVEF showed a reduction, suggesting a predominant afterload effect. This afterload effect of PEEP has already been reported along with a RV dilation [6–9], and the cause of the increase in RV volumes might be related either to a compensatory mechanism according to the Frank–Starling law (preload reserve utilization with constant contractility), or to an alteration of ventricular geometry and ejection (altered function) [10, 28], or to a decreased contractility [8, 9] due to a mismatch between increased RV work and reduced RV perfusion [11].

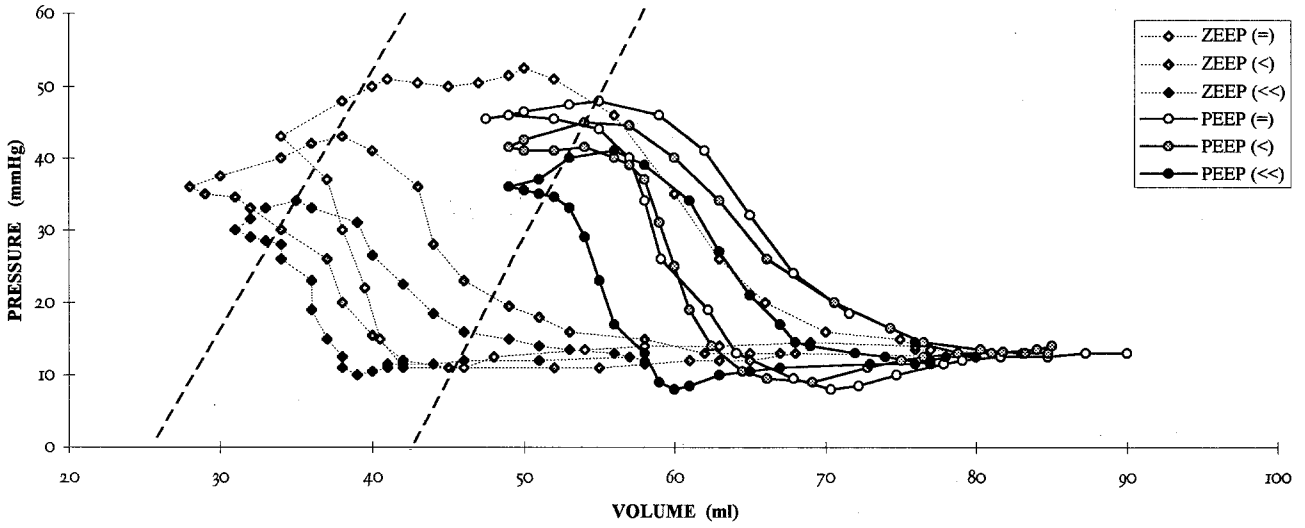
In normal dogs. Oikawa et al. [29], after producing a fourfold increase in RV afterload, observed a constant RV contractility evaluated by Emax and an increase in RVEDVI, suggesting the utilization of the preload reserve by the RV. In closed-chest dogs with experimental acute respiratory distress syndrome and pulmonary hypertension, Zwissler et al. [30] evaluated myocardial perfusion by a microsphere radiolabeled technique. They found that, during the use of 20 cmH_2O of PEEP, a significant increase of RV blood flow both in the free wall and in the right side of the interventricular septum occurred. These data [30] suggest that the increase in RV oxygen demand (caused by the PEEP-induced increase in afterload) can be matched by increased myocardial perfusion of the RV. Shulman et al. [11], in closed-chest dogs, found a decrease in CO and an increase in RVESV using 20 cmH_2O of PEEP. However, a significant RVESV increase was found only when the right coronary artery was occluded during PEEP. Therefore, a decrease in RV function might occur if RV dilation (causing an increase in oxygen demand and a decrease of subendocardial perfusion) is associated with a reduction in coronary perfusion. Thus, during PEEP, the finding of RV dilation is not per se suggestive of RV failure, and evaluation of RV contractility may be useful.

As discussed above, the PRSWI has been recently proposed for evaluating RV function and contractility. If a significant relationship between RVSW and RVEDVI is found (see group B), a constant function with unchanged contractility can be suggested. In group A, only 2 patients (5 and 6) showed a relationship between RVSWI/RVEDVI. In these 2 patients, RV dilation is likely related to the preload reserve utilization, with no alteration in contractility.

In 7 of 9 patients in group A, no significant relationship between RVSWI and RVEDVI was found (Fig. 2, top). Since the PRSW model is based on a pure preload variation, the lack of relationship suggests that contractility variations may occur during PEEP. An upward and/or leftward displacement on the $x-y$ plot should indicate an increase in myocardial performance, while a downward and/or rightward shift is suggestive of a decrease in performance. More specifically, 3 patients (2, 7, and 8) show a scattered distribution on the RVSWI/RVEDVI plot, likely due to a combined effect of preload, afterload, and contractility changes on RV performance. In 4 patients (1, 3, 4, 9), at PEEP 15 cmH_2O, RVSWI/RVEDVI data points are consistently shifted rightward from the ZEEP value. This rightward shift indicates that with PEEP the same extent of work is developed at the expense of higher RVEDV and, hence, of higher oxygen demand. Thus, PEEP may decrease RV performance.

Preliminary findings of a new study may help to clarify the results of group A. This ongoing study is based on the analysis of RV pressure/volume loop by biplane cineangiography [31]. In ARF patients, a caval balloon was inflated in order to obtain a rapid preload reduction allowing an accurate computation of Emax. The behavior of one representative patient is shown in Fig. 3. In this patient, PEEP 10 cmH_2O caused a decrease in CI and SI associated with an increase in RV volumes, a situation similar to group A in the present study. Emax was shifted to the right (i.e., higher RV volumes), but its slope did not change (i.e., same contractility). The unchanged contractility with the increase in RV volumes suggests that the decreased RV performance is likely related to an increase in afterload causing a change in RV geometry, and, hence, alterations in the ejection pattern (Fig. 3) [32].

In conclusion, this study confirms that the main cause of the reduction in CO with PEEP is a preload reduction which is associated with an unchanged RV contractility. Another mechanism to be taken into account is the increase in RV afterload, with the consequent increase in RV volumes. In this latter situation, RV performance is often decreased likely due to alterations in the ejection pattern or to a mismatch between decreased coronary flow and increased myocardial oxygen uptake. It is not possible to evaluate which is the predominant mechanism in the patients in the present study. It is the opinion of the authors that, when PEEP is applied, RV function must be evaluated in each patient, since the effects of PEEP are individually unpredictable. PEEP may help to disclose potential underlying alterations of RV preload, afterload, and contractility that, even though not clinically evident,



can contribute to a decrease in CO. Therefore, the kind of RV response to a PEEP challenge may be a guide to therapeutic strategy or a first screening before more expensive and complex diagnostic procedures are considered.

Acknowledgement The authors are grateful to Drs. A. Chiddo, S. Musci, and A. Marchese for their helpful suggestions and stimulating discussion.

Fig. 3 Right ventricular pressure–volume loops in an ARF patient. The *y*-axis shows right ventricular pressure and the *x*-axis right ventricular volume. *Diamonds* represent values at zero end-expiratory pressure *ZEEP*, while *circles* represent values at *PEEP* 10. For each level of PEEP, the open symbols represent baseline, the hatched symbols represent values after preload variation, and the closed symbols represent values with further preload decrease. The two *dotted lines* show the end-systolic pressure–volume relationships (Emax). Note that with PEEP, the slope of Emax does not change, but the relationship is only shifted to the right

References

1. Santamore W, Bove AA, Heckman JL (1984) Right and left ventricular pressure-volume response to positive end-expiratory pressure. Am J Physiol 246: H114–H119
2. Fewell JE, Abeudshein DR, Carlson CJ, Rapaport E, Murray JF (1980) Mechanisms of decreased right and left ventricular end-diastolic volumes during continuous positive-pressure ventilation in dogs. Circ Res 47:467–472
3. Fessler HE, Brower RG, Wise RA, Permutt S (1992) Effects of positive end-expiratory pressure on the canine venous return curve. Am J Respir Crit Care Med 146:4–10
4. Piene H (1986) Pulmonary vascular impedance and right ventricular function. Physiol Rev 66:606–649
5. Canada E, Benumof JL, Tousdale FR (1982) Pulmonary vascular resistance correlates in intact normal and abnormal canine lungs. Crit Care Med 10: 719–723
6. Brienza A, Dambrosio M, Bruno F, La Gioia V, Marucci M, Belpiede G, Giuliani R (1988) Right ventricular ejection fraction measurement in moderate acute respiratory failure (ARF). Effects of PEEP. Intensive Care Med 14:478–482
7. Imai T, Uchiyama M, Maruyama N, Yoshikawa D, Fujita T (1993) Influence of constant sustained positive airway pressure on right ventricular performance. Intensive Care Med 19:8–12
8. Biondi JW, Schulman DS, Soufer R, Matthay RA, Hines RL, Kay HR, Barash PG (1988) The effect of incremental positive end-expiratory pressure on right ventricular hemodynamics and ejection fraction. Anesth Analg 67: 144–151
9. Shulman DS, Biondi JW, Matthay RA, Barash PG, Zaret BL, Soufer R (1988) Effect of positive end-expiratory pressure on right ventricular performance. Am J Med 84:56–67
10. Pinsky MR, Desmet JM, Vincent JL (1992) Effect of positive end-expiratory pressure on right ventricular function in humans. Am J Respir Crit Care Med 146:661–687
11. Shulman DS, Biondi JW, Zohgbi S, Cecchetti A, Zaret BL, Soufer R (1992) Left ventricular diastolic function during positive end-expiratory pressure. Am J Respir Crit Care Med 145: 515–521
12. Jardin F (1994) PEEP and ventricular function. Intensive Care Med 20: 169–170
13. Glower DD, Spratt JA, Snow ND, Kabas JS, Davis JW, Olsen CO, Tyson GS, Sabiston DC, Rankin JS (1985) Linearity of the Frank–Starling relationship in the intact heart: the concept of preload recruitable stroke work. Circulation 75:994–1009
14. Kass DA, Beyar R, Lankford E, Heard M, Maughan WL, Sagawa K (1989) Influence of contractile state on curvilinearity of in situ end-systolic pressure-volume relations. Circulation 79: 167–178

15. Feneley MP, Skelton TN, Kisslo KB, Davis JW, Bashore TM, Rankin JS (1992) Comparison of preload recruitable stroke work, end-systolic pressure-volume and dP/dtmax-end-diastolic volume relations as indexes of left ventricular contractile performance in patients undergoing routine cardiac catheterization. J Am Coll Cardiol 19: 1522–1530
16. Karunanithi MK, Michniewicz J, Copeland SE, Feneley M (1992) Right ventricular preload recruitable stroke work, end-systolic pressure-volume, and dP/dTmax end-diastolic volume relations compared as indexes of right ventricular contractile performance in conscious dogs. Circ Res 70:1169–1179
17. Murray JF, Matthay MA, Luce JM, Flick MR (1988) An expanded definition of the adult respiratory distress syndrome. Am J Respir Crit Care Med 138:720–723
18. Teboul JL, Besbes M, Andrivet P, Axler O (1992) A bedside index assessing the reliability of pulmonary artery occlusion pressure measurements during mechanical ventilation with positive end-expiratory pressure. J Crit Care 7: 22–29
19. Kay HR, Afshari M, Barash P (1983) Measurement of ejection fraction by thermal dilution technique. J Surg Res 34:337–346
20. Assmann R, Heidelmayer CF, Trampisch HJ (1991) Right ventricular function assessed by thermodilution technique during apnea and mechanical ventilation. Crit Care Med 19:810–817
21. Vincent JL, Thirion M, Brimioulle S, Lejeune P, Kahn RJ (1986) Thermodilution measurement of right ventricular ejection fraction with a modified pulmonary artery catheter. Intensive Care Med 12:33–38
22. Spinale FG, Mukherjee R, Tanaka R, Zile MR (1992) The effects of valvular regurgitation on thermodilution ejection fraction measurements. Chest 101:723–731
23. Dunnet CV (1955) A multiple comparison procedure for comparing several treatments with the control. J Am Stat Assoc 50:1096–1121
24. Raper RF, Sibbald WJ (1992) Increased right ventricular compliance in response to continuous positive airway pressure. Am J Respir Crit Care Med 145:771–775
25. Dambrosio M, Giuliani R, Ranieri VM, Brienza N, Cinnella G, Brienza A (1993) Right ventricular function in COPD patients during acute ventilatory failure. Effects of PEEP. Am J Respir Crit Care Med 147:A608
26. Dhainaut JF (1988) Evaluation and clinical applications of right ventricular performance monitoring in the ICU. Appl Cardiopulmon Pathophysiol 2:47–57
27. Martin C, Perrin G, Saux P, Papazian L, Gouin F (1994) Effects of norepinephrine on right ventricular function in septic shock patients. Intensive Care Med 20:444–447
28. Gault JH, Ross J, Braunwald E (1968) Contractile state of the left ventricle in man: instantaneous tension-velocity-length relations in patients with and without disease of the ventricular myocardium. Circ Res 22:451–463
29. Oikawa RY, Burkhoff D, Alexander J, Sagawa K (1985) End-systolic pressure–volume relation of the right ventricle ejecting against simulated pulmonary impedance. FASEBJ 44: 1378–1387
30. Zwissler B, Schosser R, Schwickert C, Spengler P, Weiss M, Iber V, Messmer K (1991) Perfusion of the interventricular septum during ventilation with positive end-expiratory pressure. Crit Care Med 19:1414–1424
31. Dell'Italia LJ, Walsh RA (1988) Right ventricular diastolic pressure–volume relations and regional dimensions during acute alterations in loading conditions. Circulation 77:1276–1282
32. Chiddo A, Bortone A, Musci S, Marchese A, Quagliara D, Rizzo P (1991) Two phase right ventricle-afterload match. Eur Heart J 12:P367