

Silvia Nunes
Esko Ruokonen
Jukka Takala

Pulmonary capillary pressures during the acute respiratory distress syndrome

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Abstract Objectives: (1) To describe the evolution of pulmonary capillary pressure (Pcap) and of the pressure drop across the pulmonary venous bed from early to established acute respiratory distress syndrome (ARDS), (2) to assess Pcap under different levels of positive end-expiratory pressure (PEEP) and (3) to compare the visual method and a mathematical model to determine Pcap. **Design:** Prospective, intervention study. **Setting:** Intensive care unit in a teaching institution.

Patients: Nine ARDS patients, according to the ARDS Consensus Conference criteria. **Interventions:** Pulmonary arterial pressures were measured during routine respiratory mechanics measurements throughout ARDS. Four PEEP levels (6, 9, 12 and 15 cmH₂O) were studied.

Measurements and results: Pulmonary artery occlusions were made in triplicate at each PEEP level. Pcap was determined for every occlusion trace by three observers (visual method) and a mathematical model. Diastolic pulmonary artery pressure (PAPd) and pulmonary artery occlu-

sion pressure (PAOP) were measured. The visually determined Pcap showed a bias of 2.5 ± 2.1 mmHg as compared to the mathematical estimation. PAPd, Pcap and PAOP tended to decrease from early to late ARDS ($p=0.128, 0.265, 0.121$). Pcap–PAOP (6.3 ± 2.7 mmHg) did not change throughout ARDS. Higher PEEP levels were associated with increased PAPd, Pcap and PAOP, as well as with larger Pcap–PAOP throughout ARDS. **Conclusions:** Pulmonary capillary pressure cannot be predicted from PAOP during early and established ARDS. The high variability in Pcap–PAOP increases the risk for underestimation of filtration pressures and consequently the risk for lung edema. Pcap can be estimated at the bedside by either the visual or mathematical methods.

Keywords Pulmonary capillary pressure · Pulmonary artery occlusion pressure · Pulmonary circulation · Acute respiratory distress syndrome · Acute lung injury · Positive end-expiratory pressure

S. Nunes · E. Ruokonen
Critical Care Research Program,
Division of Intensive Care,
Department of Anesthesiology
and Intensive Care,
Kuopio University Hospital,
Kuopio, Finland

J. Takala (✉)
Department of Intensive Care,
Bern University Hospital—Inselhospital,
3010 Bern, Switzerland
e-mail: Jukka.Takala@insel.ch

Introduction

Pulmonary capillary pressure (Pcap) cannot be measured directly. Indirect methods seek to assess the pressure in the sites where fluid leakage occurs [1]. Since Pcap is a major determinant of fluid leakage, its importance is emphasized in the presence of increased permeability. In

ARDS, the gradient between Pcap and pulmonary artery occlusion pressure (PAOP) (Pcap–PAOP) [2, 3, 4], as well as capillary permeability [5] are increased. Evidence exists that reduction of Pcap may improve lung edema in the acute respiratory distress syndrome (ARDS) [6, 7]. Although it is physiologically obvious that PAOP is not a surrogate for Pcap in these circum-

Table 1 Demographic and clinical data of the patients

Patient (no./sex)	Age (year)	Diagnosis	Outcome	Day after ARDS diagnosis	PEEPset (cmH ₂ O)	Static compliance (ml/cmH ₂ O)	Murray [11]
1/M	28	Multiple trauma with thoracic and pulmonary contusion	Survived	1	10	67	2.75
				7	8	41	2.5
2/M	37	Wegener's granulomatosis	Died	1	12	33	3.5
3/F	47			Pneumonia	Survived	1	10
						9	10
4/M	36	Pneumonia	Survived	1	10	35	3.25
						8	7
5/M	17	Pneumonia	Survived	3	10	58	2.5
						5	8
6/M	42	Acute hemorrhagic pancreatitis	Died	3	6	38	3
						7	6
7/F	70	Perforated duodenal ulcer; septic shock	Survived	1	8	30	2.75
8/M	49			Pneumonia; septicemia	Survived	1	6
						6	6
9/M	22	Acute pancreatitis	Survived	3	6	24	3

M male, *F* female, *PEEPset* positive end-expiratory pressure setting

stances, Pcap is seldom assessed and PAOP is commonly used to guide fluid management in ARDS. The protective approach to ventilation in ARDS advocates high positive end-expiratory pressure (PEEP) levels and low tidal volumes [8]. The effect of PEEP on Pcap and on Pcap–PAOP remains unsettled. Since Pcap–PAOP is not constant, hydrostatic pressure in the capillaries may be grossly underestimated in the clinical setting.

We hypothesized that, in ARDS, Pcap–PAOP varies over time and with PEEP level. We evaluated the evolution of Pcap and Pcap–PAOP from early to established ARDS. In addition, we assessed the effect of PEEP on Pcap and Pcap–PAOP. Pcap was determined using two different methods. The reproducibility and between-method variability of computed Pcap were evaluated.

Methods

Patients

Nine ARDS patients [9] were studied. Measurements were made during acute ARDS (1–3 days after diagnosis), and repeated later (5–9 days after diagnosis), in six patients. The study was approved by the Ethics Committee. The need for informed consent was waived since the measurements required no additional instrumentation and the assessment of Pcap was performed in conjunction with routine measurements of respiratory mechanics [10]. Patients were intubated and ventilated under controlled mode (Servo 900, Siemens-Elcoma, Sweden). All patients had a pulmonary arterial catheter in place for clinical purposes. Initial ventilator settings were determined by the attending physician (setVt, PEEPset). Demographic and clinical data [11] are presented in Table 1.

Material

A heated pneumotachometer (Fleisch No2, Switzerland) and two differential pressure transducers (Validyne, MP45, ± 2.0 and ± 100.0 cmH₂O; CA) were used for flow and airway opening pressure measurements. Volume was obtained by digital integration of the flow signal. Systemic and pulmonary artery pressures (SAP, PAP) and central venous pressure (CVP) were obtained from a patient monitor (AS3, Datex-Ohmeda, Finland). A physiologic recording system (Direc, Raytech Instruments, Canada) was used.

Protocol

Four PEEP levels (6, 9, 12 and 15 cmH₂O) were used for the assessment of respiratory mechanics and, at each PEEP level, three tidal volumes (Vt) were used (setVt, a 20% higher Vt and a 20% lower Vt). Pcap measurements were made only at setVt, by occluding the pulmonary artery in triplicate for a minimum of 6 s during an end-expiratory pause. Static pressures were measured and static compliance of the respiratory system calculated at each ventilator setting by the occlusion method [12].

Analysis

Three intensive care specialists estimated Pcap using the visual inspection method [13] (Fig. 1A). This method has been validated and used experimentally and clinically [1, 2, 13]. The mathematical method chosen [14, 15] has been validated against the double occlusion method [1, 15]. We superimposed one non-occluded pulmonary artery pressure curve to the occluded curve and defined

Fig. 1 **A** Visual inspection method for estimation of pulmonary capillary pressure (P_{cap}); **B** Mathematical method for the estimation of P_{cap}

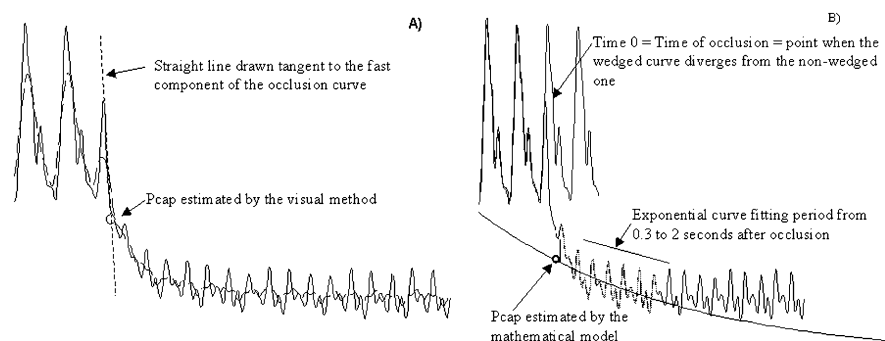


Table 2 Pulmonary capillary pressure (P_{cap} ; means \pm SD)

P_{cap} (mmHg)		Obs. mean	No.	Exp0.3–2 (0.2)	No.	Exp0.5–2 (0.3)	No.
Acute ARDS	PEEP6	17.4 \pm 4.9	20	14.6 \pm 4.3	20	13.4 \pm 3.7	20
	PEEP9	18.6 \pm 4.1	21	14.6 \pm 3.8	21	14.0 \pm 3.4	21
	PEEP12	19.5 \pm 4.3	22	16.9 \pm 3.9	22	15.6 \pm 3.6	22
	PEEP15	19.2 \pm 4.5	21	16.5 \pm 3.6	21	15.1 \pm 3.5	21
	Total	18.7 \pm 4.5	84	15.7 \pm 4.0	84	14.5 \pm 3.6	84
Late ARDS	PEEP6	15.2 \pm 3.0	18	13.2 \pm 2.6	18	11.6 \pm 2.3	18
	PEEP9	15.0 \pm 2.4	15	13.2 \pm 3.2	15	11.9 \pm 2.6	15
	PEEP12	16.2 \pm 2.7	15	14.8 \pm 3.1	15	13.5 \pm 2.9	15
	PEEP15	17.5 \pm 2.3	14	16.0 \pm 3.1	14	14.7 \pm 2.8	14
	Total	15.9 \pm 2.7	62	14.2 \pm 3.1	62	12.8 \pm 2.8	62
Total		17.5 \pm 4.0	146	15.1 \pm 3.7	146	13.8 \pm 3.4	146

Obs mean mean values of P_{cap} estimated by the three observers (visual method), *Exp0.3–2 (0.2)* exponential fitting from 0.3 to 2 s after occlusion extrapolated to 0.2 s after occlusion, *Exp0.5–2 (0.3)*

exponential fitting from 0.5 to 2 s after occlusion extrapolated to 0.3 s after occlusion, *ARDS* acute respiratory distress syndrome, *PEEP* positive end-expiratory pressure

the moment of occlusion as the moment when the occluded pressure deviated below the non-occluded tracing [16] (Fig. 1B). We fitted an exponential curve to the pressure signal at two different time periods after occlusion, 0.3–2.0 s as proposed by Hakim [15] (Fig. 1B) and 0.5–2.0 s. As extrapolation to time zero was shown to overestimate P_{cap} [17], we used extrapolation to 0.2 s after occlusion for the fitting period comprised between 0.3 and 2 s. This value approximates the most accurate extrapolation time point (152 ms after occlusion) from mono-exponential fitting [18]. An arbitrary extrapolation to 0.3 s was used with the fitting from 0.5 to 2 s. The mean PAP during the sixth second after occlusion was used as PAOP. The pressure drop across the pulmonary venous bed (P_{cap} –PAOP) was expressed as a fraction of the total pressure drop across the pulmonary vascular tree (PAPd–PAOP): $[(P_{cap}$ –PAOP)/(PAPd–PAOP)] [16]. P_{cap} values determined by the three observers were averaged. Values obtained from the occlusions carried out in triplicate were averaged and used to evaluate the pressure changes across the pulmonary vasculature.

Statistics

Inter-observer and intra-observer coefficient of variation were respectively computed for P_{cap} estimated by the three observers for the same occlusion and for the occlusions carried out in triplicate. A Bland-Altman plot assessed the differences between P_{cap} analysis methods [19]. The between-method differences and effect of PEEP were assessed by multiple analysis of variance for repeated measures (SPSS for Windows). Values are presented as means \pm SD. A probability value of 0.05 or less was considered significant.

Results

Pulmonary artery occlusions were performed in triplicate at 59 time points, $n=176$ (one missing value). Thirty curves (17%) were excluded due to spontaneous respiratory efforts ($n=18$), underdamping of the pulmonary artery pressure curve ($n=4$) and start of the pulmonary artery occlusion before the expiratory pressure plateau ($n=8$).

Pulmonary capillary pressure values are shown in Table 2. Differences between observers were small

Fig. 2 Bland-Altman plot comparing mean pulmonary capillary pressure (*Pcap*) obtained by the visual method to *Pcap* values obtained by the mathematical method. Agreement (r^2) between methods was 0.74

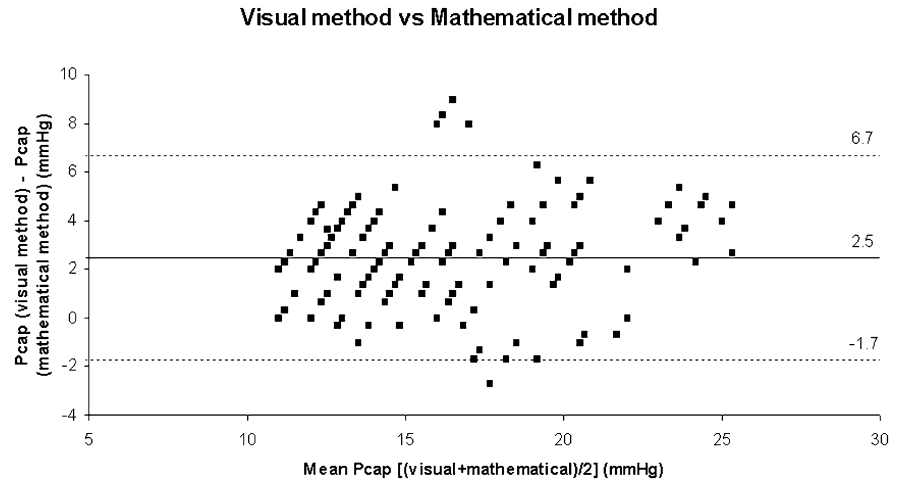


Table 3 Hemodynamic data of the patients

Patient (No./sex)	Day after ARDS diagnosis	CO (l/min)	PAOP ^a (mmHg)	PAPd-PAOP ^a (mmHg)	Visual Pcap ^a (mmHg)	Math. Pcap ^a (mmHg)	PVR (dyne . sec/cm ⁵)	VenR/PVR
1/M	1	12.5	7.7	13.3	14.6	10.8	84.72	0.23
	7	9.9	7	13	15.7	12.1	104.70	0.39
2/M	1	8.4	15	15.3	26.7	22.2	145.45	0.47
3/F	1	3.2	— _b	— _b	— _b	— _b	— _b	— _b
	9	3.9	6.7	10.3	15	11	211.79	0.42
4/M	1	12.5	10.7	11.6	19.2	12.9	74.33	0.19
	8	7.1	6.3	16	20.3	15.3	179.82	0.56
5/M	3	12	11	7.3	15.1	13.3	48.75	0.31
	5	9.8	9	5.3	12.4	10.1	43.16	0.22
6/M	3	11.9	7	7	12.1	10.3	47.15	0.47
	7	8	10	8.3	16.4	16.4	83.12	0.77
7/F	1	4	10.3	17.5	21.8	18	350.05	0.46
8/M	1	7.2	14	7	19	18.8	77.52	0.68
	6	6.5	6	6	11.1	11	73.53	0.84
9/M	3	8.4	14.3	9.7	20.9	17.3	91.91	0.31

M male, *F* female, *ARDS* acute respiratory distress syndrome, *CO* cardiac output, measured prior to positive end-expiratory pressure (*PEEP*) manipulations, *PAOP* pulmonary artery occlusion pressure, *PAPd* diastolic pulmonary artery pressure, *Pcap* capillary pulmonary pressure, *PVR* pulmonary vascular resistance [(*PAPd*-

PAOP)/*CO*], *VenR/PVR* venous pulmonary vascular resistance / total pulmonary vascular resistance

^a Values obtained during the *PEEP* level closest to *PEEP*set

^b Data excluded due to artifacts during the pulmonary arterial pressure recordings

(0.3 ± 1.7 mmHg; 95%CI 0.16 mmHg) but consistent ($p=0.022$). Mathematical estimations also showed small (1.2 ± 0.9 mmHg; 95%CI 0.14 mmHg), consistent differences ($p<0.001$). The exponential fitting from 0.5 to 2 s after occlusion did not help to avoid artifacts as compared to the model including a longer fitting. Only the latter was used for further analysis. The visual approach showed a bias of 2.5 ± 2.1 mmHg as compared to the mathematical method (Fig. 2). Intra-observer coefficient of variation for the visual method ranged from $4.2 \pm 3.2\%$ to $6.3 \pm 5.4\%$ and was $5.0 \pm 4.6\%$ for the mathematical model. Inter-observer variability was $5.6 \pm 4.1\%$.

Hemodynamic data are presented in Table 3. *PAPd*, *Pcap* and *PAOP* tended to decrease towards late *ARDS* ($p=0.128$, 0.265, 0.121) (Fig. 3). *Pcap*–*PAOP* did not change throughout *ARDS* (7.7 ± 2.7 vs 7.6 ± 2.9 mmHg—

visual method; 4.7 ± 2.4 vs 5.8 ± 2.4 mmHg—mathematical method). *PAPd*, *Pcap*, *PAOP* and *Pcap*–*PAOP* increased with *PEEP* throughout *ARDS* (Fig. 3). (*Pcap*–*PAOP*)/(*PAPd*–*PAOP*) tended to increase during established *ARDS* ($p=0.085$) and with *PEEP* ($p=0.101$) (*PEEP*-phase of *ARDS* interaction: $p=0.029$) (Fig. 3).

Discussion

We found that: (1) *PAPd*, *Pcap* and *PAOP* decreased from acute to established *ARDS*, while *Pcap*–*PAOP* remained unchanged, (2) *Pcap* and *Pcap*–*PAOP* increased with *PEEP* throughout *ARDS* and (3) *Pcap* can be estimated at the bedside by either the visual or the mathematical method.

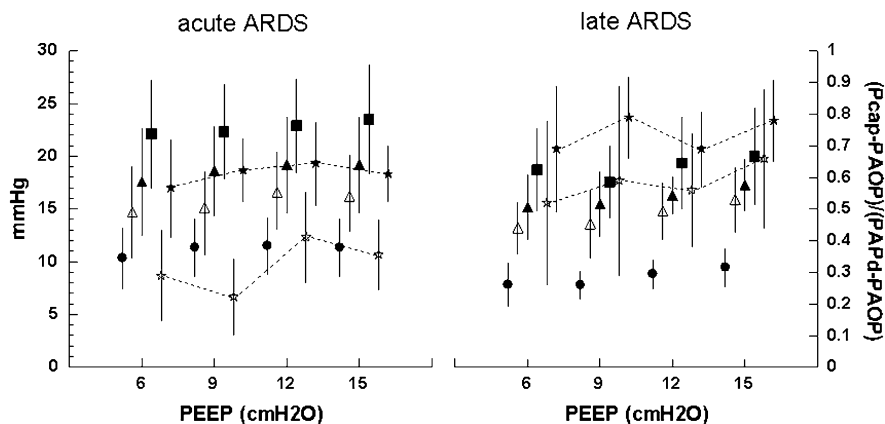


Fig. 3 Left Y axis (for both acute and late ARDS): Pulmonary artery occlusion pressure (PAOP; circles), pulmonary capillary pressure (Pcap; visual method = filled triangles; mathematical method = open triangles) and diastolic pulmonary artery pressure (PAPd; squares). Right Y axis (for both acute and late ARDS): (symbols connected by a dotted line) venous component of the pressure drop across the pulmonary vasculature (Pcap–PAOP)/(PAPd–PAOP)—(Pcap determined by the visual method = filled stars; Pcap determined by the mathematical method = open stars) at different positive end-expiratory pressure (PEEP) levels during the acute and late stage of acute respiratory distress syndrome (ARDS)

Methodological analysis

Direct measurement of Pcap in patients is not possible, but surrogate estimates can be obtained. Analysis of the post-occlusion pulmonary artery pressure trace is based on a model of pulmonary vasculature which does not include the resistive component of pulmonary capillaries. Some degree of Pcap overestimation can therefore be expected.

The slow inflation of the Swan-Ganz balloon decreases the initial slope of the occlusion curve and the separation between the instantaneous drop and the slower phase is not always self-evident [15]. This may explain the higher values computed by the visual method (which uses the initial slope) as compared to the mathematical method (which uses the unaffected slower phase) (2.5 ± 2.1 mmHg). Despite this, the two techniques had similar variability. Comparable between-method differences and variability have been reported previously [3, 4, 13]. Our data comprise traces with the pulmonary artery occlusion happening in every phase of the heart cycle. Inaccuracies may originate here, both due to the accentuated initial “fast component” occurring during systole [15] and due to a less accurate identification of the time of occlusion during diastole [18]. However, Pcap estimations were obtained in triplicate at each PEEP level and averaged for clinical analysis—a practice similar to the measurement of cardiac output.

Clinical analysis

To our knowledge, no data exist on the evolution of Pcap and Pcap–PAOP with PEEP and throughout ARDS. Our results show large, highly variable Pcap–PAOP values throughout ARDS. (Pcap–PAOP)/(PAPd–PAOP) tended to rise during established ARDS (Fig. 3) despite decreased cardiac output. This rise may be due to a larger decrease of PAP and PAOP as compared to Pcap from the acute to the late phases of ARDS, possibly caused by a “dry-lung” approach to fluid management in our unit. PAP, Pcap, PAOP and pulmonary venous resistances have been shown to increase with PEEP [20, 21]. Our data suggest a similar behavior of Pcap and Pcap–PAOP with increasing PEEP during ARDS (Fig. 3). Unfortunately we have no data on the effect of PEEP on blood flow. If anything, PEEP would be expected to decrease cardiac output and thereby attenuate an increase in Pcap–PAOP. Since the number of patients studied was small, especially in the arbitrarily defined late phase, conclusions on the time course of Pcap throughout ARDS cannot be drawn. Despite high inter-individual variability, our data demonstrates that high Pcap may be present in established ARDS.

Assuming that elevated Pcap contributes to lung edema in ARDS, highly variable Pcap–PAOP in ARDS may lead to underestimation of the risk for lung edema. This and the variability of Pcap throughout ARDS should be taken into consideration when manipulating filling pressures. Both the visual and mathematical methods of estimating Pcap are suitable for bedside use.

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