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*Critical Care* 2012, **16**:R1 doi:10.1186/cc10599

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**ISSN** 1364-8535

**Article type** Research

**Submission date** 17 August 2011

**Acceptance date** 3 January 2012

**Publication date** 3 January 2012

**Article URL** <http://ccforum.com/content/16/1/R1>

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# **Extravascular lung water index improves the diagnostic accuracy of lung injury in patients with shock**

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## Abstract

**Introduction:** The diagnosis of acute lung injury may be more robust if more accurate physiological markers can be identified. Extravascular lung water (EVLW) is one possible marker, and has been shown to correlate with respiratory function and mortality in patients with sepsis. Whether EVLW confers diagnostic value in a general population with shock, and which index performs best is unclear. We investigated the diagnostic accuracy of various EVLW indices in patients with shock.

**Methods:** Prospective, observational cohort study of 51 patients admitted to a tertiary ICU with shock. EVLW was measured within 6 hours of ICU admission and indexed to actual weight (EVLW/ABW), predicted body weight (EVLW/PBW) and pulmonary blood volume (EVLW/PBV). Their relation to the diagnosis and severity of lung injury and intensive care unit (ICU)-mortality were studied. Positive and negative likelihood ratios, pre- and post-test odds for a diagnosis of lung injury and mortality were calculated.

**Results:** All EVLW indices were higher among patients with lung injury and significantly correlated with respiratory parameters. Further, all EVLW indices were significantly higher in nonsurvivors. Using EVLW improves the post-test odds ratio for the diagnosis of acute lung injury (ALI), acute respiratory distress syndrome (ARDS) and severe lung injury (sLI) by up to 8-fold. Combining increased EVLW and a diagnosis of ALI, ARDS or sLI increases the post-test odds of ICU-mortality. EVLW/ABW and PBV gave the best diagnostic performance in this population.

**Conclusions:** EVLW was associated with degree of lung injury and mortality, regardless of the index used, confirming that it may be used as a bedside indicator for disease severity. Using EVLW as a bedside test conferred added diagnostic value for the identification of patients with lung injury.

**Keywords:** ARDS, ALI, extravascular lung water, sepsis, shock, pulmonary oedema, likelihood ratio

## Introduction

Extravascular Lung Water (EVLW) is an estimation of the fluid in the pulmonary interstitium and alveolar space[1]. In Intensive Care Units (ICUs), EVLW is usually obtained as one of the parameters in the PiCCO ((PiCCOplus®, PULSION Medical Systems, Munich, Germany) monitor, using a transpulmonary thermodilution technique. EVLW may be used as a bedside indicator of extravascular leakage, for example during acute lung injury (ALI)[1-7], although this requires further confirmation.

The present study was driven by current limitations in diagnosis and prognosis of ALI and ARDS. For example, the North-American European Consensus Conference (NAECC) criteria may be too insensitive for identifying 'subclinical ARDS'. Conversely, its specificity has also been questioned since some patients identified by these criteria no longer fulfill the criteria for ARDS after 24 hours on mechanical ventilation[8]. Further, it is known that Murray's Lung Injury Score (LIS) and  $\text{PaO}_2/\text{FiO}_2$  lack sensitivity for predicting mortality[9] although they are clearly indicative of lung injury. It has been proposed that the diagnosis and prognosis of lung injury may be more robust if more accurate physiologic markers can be identified. EVLW has been proposed as one such method[10-12] and there are a number of studies attesting to the value of EVLW for clinical outcome prediction[2,4,5,13-17].

In previous studies, EVLW has mainly been investigated within the context of sepsis and septic shock, and seems to be associated with severity of respiratory dysfunction and mortality[2,4,5,7,15-17]. However, ALI and ARDS may also occur in patients without sepsis. Thus it is relevant to study EVLW in larger populations at high risk of developing the disease. This would encompass critically ill patients with systemic inflammation due to any cause (septic and non-septic) and shock. It is also unclear which EVLW index is the most useful measure. Most reports regarding EVLW have used an index based on the actual body weight (ABW). Three recent studies indicate that using predicted body weight (PBW) may be a better predictor of survival and disease severity[2-4]. Indexing EVLW to PBW instead of ABW has been shown to improve the correlation between EVLW and Murray's Lung Injury Score and  $\text{PaO}_2/\text{FiO}_2$ [3]. EVLW indexed to Pulmonary Blood Volume (PBV) is another index and is thought to reflect increased hydrostatic pressure and pulmonary permeability[5-7,18]. It has been proposed as a useful index for differentiating between the two mechanisms of increased EVLW[18].

These considerations led us to ask the following questions: In a critically ill population with shock and at risk for developing lung injury, 1) how well do different EVLW indices measure the severity of lung injury? 2) how well do the different EVLW indices relate to ICU-mortality? 3) by applying EVLW as a bedside test, can we increase our chances of diagnosing lung injury? We investigated various indices of EVLW in relation to the presence and severity of lung injury and ICU-mortality. Finally, we investigated the diagnostic value of the various indices for ALI, ARDS and severe lung injury, as defined by NAECC criteria and LIS respectively.

## **Materials and methods**

The study was approved by the Regional Ethical Review Board, Lund, Sweden (Dnr.187/2005).

Informed consent was sought either from the patient or, if not possible, from the next of kin.

The study design was a single-centre prospective observational cohort study of critically ill patients admitted to the mixed-bed ICU of Skåne University Hospital, Malmö, Sweden. Fifty-five consecutive patients with the Systemic Inflammatory Response Syndrome (SIRS) and shock despite fluid resuscitation were included. Specifically, patients were aged over 18, SIRS criteria[19] and exhibited circulatory failure, defined as failure to maintain mean arterial pressure  $\geq 70$  mmHg despite adequate fluid resuscitation according to the surviving sepsis campaign algorithm[20]. Exclusion criteria were pregnancy, abnormalities of coagulation, fibrinolytic therapy, compromised immunity or a “Do Not Attempt Resuscitation” order. Patients could only be included once.

Sepsis was defined according to the criteria published by Bernard et al[21]. ALI and ARDS were defined by the criteria set by the NAECC[22]. Severe lung injury (sLI) was defined using the lung injury score (LIS) proposed by Murray[23], with severe lung injury indicated by a score of  $>2.5$ . Acute Physiology and Chronic Health Evaluation (APACHE) II scores[24] were calculated at admission and Sequential Organ Failure Assessment (SOFA) scores[25] were calculated for each day of the study period. Ventilator settings (Dräger Evita XL, Lübeck, Germany) including positive end expiratory pressure (PEEP) and inspiratory oxygen concentration ( $FiO_2$ ) were recorded, and if the patient was not mechanically ventilated,  $FiO_2$  was obtained from conversion according to common tables[26]. An arterial blood sample was obtained every 6 hours. A bedside chest X-ray (CXR) was performed at

inclusion and thereafter at the treating physician's discretion. X-rays were analyzed for quadrants of alveolar consolidation (CXR score) as part of the LIS calculation[23].

All patients were initially treated according to international guidelines for the management of sepsis and septic shock[20]. This was applied to all patients at study inclusion since we were not able to identify at the outset all patients suffering from sepsis. After the initial resuscitation period, fluids were given at the treating clinician's discretion. Regardless of shock aetiology, ventilator settings were set at 6-8 ml/kg of predicted body weight. Permissive hypercapnia was accepted. PEEP was adjusted to maximize compliance and oxygenation using a decremental PEEP trial. Recruitment was performed at the clinician's discretion. Patients were monitored according to standard ICU routines but also received a 5 Fr femoral artery catheter (PV2015L20N, Pulsion Medical Systems, Munich, Germany) and, if not already existing, a central venous catheter inserted in the internal jugular or subclavian vein.

PiCCO calibration and analysis was performed within the 6 hours of study inclusion using mean values from three 20mL iced saline injections. The method is based on measurement of temperature change over time in the femoral catheter after injection of cold saline solution into the central venous catheter. The transpulmonary thermodilution curve obtained is then analyzed to calculate the cardiac output using the Stewart-Hamilton algorithm. Intrathoracic thermal volume (ITTV) and the pulmonary thermal volume (PTV) are derived from the mean transit time and the exponential downslope time of the thermodilution curve. From these volumetric variables including EVLW may be estimated; its derivation has been previously described in detail[1,14-16]. Measurements made within the first six hours of study inclusion made up the dataset for this study.

EVLW was indexed to ABW, PBW and PBV. PBW was calculated as  $50+0.91(\text{centimeters of height}-152.4)$  for males, or  $45.5+0.91(\text{centimeters of height}-152.4)$  for females. We studied these EVLW indices within 6 hours of study inclusion. The relationship between EVLW indices and respiratory parameters (presence of ALI and ARDS, sLI,  $\text{PaO}_2/\text{FiO}_2$ , CXR score and PEEP) and ICU-mortality were examined.

### **Statistical analysis**

Sample size was powered to detect a minimum difference between survivors and non-survivors of 2ml/kg of EVLW with a standard deviation of residuals of 2 ml/kg,  $\alpha = 0.05$  and  $\beta = 0.8$  using a t-test. This gave a sample size of 17 patients, however, as we were unsure of the variability of data, and based on sample sizes in previous studies, we tripled our sample size. Data are presented as median values(lower quartile:upper quartile). For correlation between two variables, Spearman's rank correlation was used and for differences between two groups, Mann-Whitney's U-test was used. For comparison of multiple groups, ANOVA on ranks was used, with a Bonferonni correction applied. Testing of proportions was made using the Fisher's Exact test. Significance was set at  $p < 0.05$ . Normality was tested for using the Kolmogorov-Smirnov test. The analyses were performed using SPSS 16.0 and SigmaStat 3.5 for Windows.

For the evaluation of the diagnostic accuracy of each EVLW index we calculated the positive (LR+) and negative (LR-) likelihood ratios, where LR+ is the sensitivity/(1-specificity), and LR- is (1-sensitivity)/specificity. The pre-test odds of disease is given by  $p/(1-p)$ , where p is the probability of the disease in the current population. The post-test odds given a positive test is the product of the LR+ and pre-test odds, whereas the post-test odds given a negative test is the product of the LR- and the pre-test odds.

## Results

The original study included 55 consecutive patients. Two were excluded due to lack of consent. Two other patients never received a femoral catheter because of technical difficulties (one with morbid obesity and one had undergone massive aorto-femoral surgery) and were excluded from further analysis. In the remaining 51 patients we experienced no major technical difficulties and no significant adverse events. At the time of inclusion we managed to obtain EVLW from 86% of the patients, and after 6 hours we had at least one measurement from all included patients. The patients' baseline characteristics are shown in Table 1. Thirty-four (67%) of patients had septic shock according to the predefined criteria[21]. The remaining 17 patients suffered from shock due to other causes, including pancreatitis (5 patients), post-major non-cardiac surgery (5 patients), intoxication and multiorgan failure (2 patients), gastrointestinal bleeding and portal hypertension (1 patient). In 4 patients the cause of shock and organ failure were never established, although sepsis could not be ruled out.

Population characteristics and clinical parameters are shown in Table 1.

### **EVLW and respiratory function**

18/51 (35%) and 15/51 (29%) patients fulfilled the NAEEC criteria for ALI and ARDS respectively. In contrast, only 9 (18%) patients fulfilled the criteria for sLI according to Murray's LIS.

The different EVLW indices were modestly correlated with PaO<sub>2</sub>/FiO<sub>2</sub> ( $r=-0.371$  to  $-0.487$ ,  $p=0.001$  to  $0.007$ ) and CXR score ( $r=0.255$  to  $0.455$ ,  $p=0.002-0.09$ ) but not with PEEP.

Patients with increased EVLW indexed to body weight ( $>10$  mL/kg) had significantly lower oxygenation than those with normal EVLW - 149(111:234) vs 246(192:301),  $p=0.006$  for EVLW/ABW; 158(121:241) vs 256(198:302),  $p=0.004$  for EVLW/PBW. Similar results were seen for EVLW/PBV - 193(143:282) vs 270(220:289),  $p=0.03$ . EVLW indexed to actual and predicted body weights were significantly higher in patients with ALI and ARDS (Figures 1a & 1b). EVLW indexed to PBV also higher in these patients (Figures 2a & 2b). There were significant incremental increases in EVLW indices with each increasing strata of the LIS score (Figure 3).

### **EVLW and mortality**

All three EVLW indices were significantly higher in nonsurvivors. EVLW/ABW 7.4(5.9-9.4) vs 9.1(7.9-12.9),  $p=0.02$ ; EVLW/PBW 9.1(7.2-11.6) vs 10.6(9.5-13.0),  $p=0.05$ ; EVLW/PBV 1.6(1.3-2.0) vs 2.0(1.6-2.6),  $p=0.03$  for survivors vs nonsurvivors respectively (Figure 4).

The corresponding positive and negative likelihood ratios, pre- and post-test odds of death given a positive EVLW test are shown in Table 2.

### **Diagnostic value of EVLW**

Depending on which index was used, EVLW identified between 44% and 100% of all patients with sLI (LIS $>2.5$ ), 27-33% of those with ALI, and 33-38% of those with ARDS.

The sensitivities, specificities, positive and negative likelihood ratios, pre- and post-test odds for making a diagnosis of ALI, ARDS or sLI using various extravascular lung water indices are shown in Table 3. By applying EVLW measurement as a bedside test, the post-test odds ratio for the diagnosis

of ALI and ARDS increased >3-fold when using EVLW/ABW (from 0.55 to 1.8 for ALI, from 0.42 to 1.33 for ARDS). When using the same index the post-test odds ratio for severe lung injury increased 2-fold.

In comparison, using EVLW/PBV as a bedside test increased the post-test odds ratio for ALI and ARDS by 1.8 and 1.6 x respectively, whereas the post-test odds ratio for severe lung injury increased by >8-fold. The post-test odds ratio for lung injury by any definition decreased markedly given a negative EVLW test.

## **Discussion**

Our main finding was that increased EVLW adds diagnostic value in identifying patients with lung injury. Further, it was significantly associated with disease severity and mortality. These findings support previous studies where EVLW was found to be useful in characterizing the severity of respiratory disease in patients with sepsis and with ARDS[2-5,15-18,27]. We now show that measurement of EVLW early during ICU admission in wider population of critically ill patients at risk of developing lung injury is of both diagnostic and clinical significance. This was seen for all EVLW indices.

As a bedside test, EVLW/PBV provided excellent diagnostic accuracy for identifying patients with severe lung injury according to Murray's LIS. For the diagnosis of ALI and ARDS, EVLW/ABW performed best, demonstrated by higher positive likelihood ratios. The application of increased EVLW as a bedside test improved the diagnostic accuracy for ALI, ARDS and sLI with 2 to 8-fold increases in the post-test odds ratio in this population. Importantly, a negative EVLW test markedly decreases the odds ratio of lung injury diagnosis, helping rule out disease[28].

'Ruling in' disease may not translate to real clinical outcomes, hence there is a need to further assess the utility of EVLW in these terms. The present study not only shows that EVLW measured early during ICU admission may be used as a marker of respiratory dysfunction in patients with shock, but that EVLW is also increased in nonsurvivors. This is consistent with earlier studies in patients with sepsis and ARDS[2-5,15-18] and extends current knowledge by showing that the post-test odds ratio for mortality increases when using EVLW as a diagnostic test, giving this test clinical relevance. This is

particularly true when combined with a prior diagnosis of ALI, ARDS or sLI, where the odds for mortality increased even further. The clear relationship between EVLW and several indicators of respiratory function, as well as mortality seen in this study support the utility of this bedside index for improved diagnosis and risk stratification early during ICU admission.

Theoretically, predicted body weight seems to be a more logical index than actual body weight, since lung volumes do not increase with body fat. Since many critically ill patients are overweight[29] EVLW/PBW should theoretically be a better index. Although we found significant correlations between EVLW/PBW and respiratory function, it demonstrated a weaker statistical relationship to mortality than EVLW/ABW or PBV. These results are in contrast to previous findings where indexing with PBW improved disease characterization and correlations with survival[2-4]. One explanation for this is that our population was not grossly overweight, with a median BMI of 25.8 kg/m<sup>2</sup>. Further, there were significant differences in BMI between survivors and non-survivors, with the latter having lower BMI values, hence confounding any possible effect of adjustment for overweight. Lastly, this study was conducted in a heterogeneous population at risk for developing lung injury, whereas previous studies have investigated populations with established ARDS[2-4].

Another theoretically attractive index to use is EVLW/PBV[6,7,18]. This index differs from EVLW adjusted for body weight in that it is thought to reflect increased lung water due to excessive hydrostatic pressure and vascular permeability independently of fluid status[6,7]. A recent study suggests that EVLW/PBV may even be useful for differentiating hydrostatic and pulmonary permeability mechanisms of increased extravascular lung water[18]. EVLW/PBV consistently produced the lowest negative likelihood ratios compared to the other indices, reinforcing its usefulness for ruling out disease[28]. Against the 'gold standard' of sLI using Murray's LIS, EVLW/PBV performed well as a diagnostic test, with excellent positive and negative likelihood ratios. For the post-test odds of mortality, EVLW/PBV did not perform better than EVLW/ABW.

How may these results be applied clinically? Firstly, we believe that EVLW may be used as an adjunct in the characterization of severe lung injury. There has been much debate regarding the usefulness of the NAEECC criteria and the lack of specificity of LIS and PaO<sub>2</sub>/FiO<sub>2</sub> in predicting mortality, leading to a search for more 'objective' criteria for ARDS[11] and for assessing the severity of lung injury[8].

Although this is not the first study reporting a relationship between EVLW and mortality, we show by calculating the positive likelihood ratios and post-test odds[28] that increased EVLW confers additional diagnostic value for the identification of patients with lung injury, and raises the odds for mortality, supporting its clinical relevance. This is particularly true when combined with a diagnosis of ALI, ARDS or sLI. This relationship is present already at an early stage (within 6 hours of study inclusion), is the first to document a stepwise relationship with deteriorating lung function. It also shows that this applies to a population with shock, and not only in patients with confirmed sepsis and/or ARDS. Early and correct identification of severely lung-injured patients at high risk of death allows the application of different treatment strategies, and facilitates the design of clinical trials based on more robust criteria, issues previously identified as important areas for future research[8].

There were a number of limitations to our study. This study by design, cannot definitively answer the question of whether EVLW is a *better* diagnostic test than the NAECC and LIS criteria, since this would have to be compared to a gold standard which does not, at present, exist. Although power calculations have been based on previously available data, our sample size is still relatively small. A larger study would have allowed us to conduct multivariate regression analysis to establish whether EVLW is an independent risk factor for mortality, as in Craig et al[4]. Although we used a pragmatic definition of sepsis[21], we cannot exclude that some of the patients in the non-septic shock group have in fact also suffered from sepsis. Further, this group represents only a limited proportion of the study and a larger numbers may have influenced the results. The study was not designed to investigate possible pathophysiological differences between EVLW/PBV and EVLW indexed to body weight, There is a mathematical coupling between intrathoracic thermal and blood volumes, on which EVLW calculation is dependent. These and unaccounted heterogeneous changes in ventilation and perfusion may have influenced the results. Lastly, we sought only to be hypothesis-generating in this prospective, observational study and therefore cannot give mechanistic explanations regarding EVLW and its relationship to clinical outcome. Studies evaluating the incremental value of adding EVLW to current diagnostic criteria for the prognosis of clinical outcome would also be a logical next step for future research.

## **Conclusions**

In this study of critically ill patients with systemic inflammation and shock, EVLW measured early during the course of disease was correlated to respiratory function. Using EVLW as a bedside test conferred added diagnostic value for the identification of patients with lung injury. Further, increased EVLW was related to severity of lung disease and mortality, confirming the results of previous studies in patients with ALI/ARDS and sepsis. Combining increased EVLW and a diagnosis of ALI, ARDS or sLI increases the post-test odds of ICU mortality. EVLW/ABW and PBV gave the best diagnostic performance in this population.

Prospective studies evaluating the value of adding EVLW to current diagnostic criteria for the prognosis of clinical outcome in at-risk populations, and as a basis for tailored interventions are logical proposals for future research.

## **Key messages**

- EVLW is significantly related to the severity of lung injury and mortality in patients with shock, regardless of which index is used
- Increased EVLW confers additional diagnostic value for lung injury
- Increased EVLW increases the odds of mortality, especially when combined with a diagnosis of ALI, ARDS and sLI
- EVLW indexed to actual body weight and pulmonary blood volume gave the best diagnostic and prognostic performances in this population

## **Abbreviations**

ABW: actual body weight; ALI: acute lung injury; ARDS: acute respiratory distress syndrome; BMI: body mass index; CXR: chest X-ray; EVLW: extravascular lung water; ICU: Intensive Care Unit; LIS: Lung Injury Score; LR+: positive likelihood ratio; LR-: negative likelihood ratio; NAEECC: North American-European Consensus Conference; PBV: pulmonary blood volume; PBW: predicted body weight; PEEP: positive end expiratory pressure; Post-test odds +: post-test odds of disease given positive test; Post-test odds -: post-test odds of disease given negative test; SIRS: systemic inflammatory response syndrome; sLI: severe lung injury.

## Competing interests

Michelle S Chew has received travel reimbursements from Pulsion Medical Systems, Germany.

## Authors' contributions

MC conceived the study, participated in study design, data collection, statistical analysis and drafted the manuscript. LI participated in data collection, statistical analysis, data interpretation and drafting of the manuscript. JD and AE participated in study design, data collection and manuscript revision. JU participated in data analysis and interpretation, and manuscript revision. LB, JR, EÅ and ML participated in data acquisition and manuscript revision. All authors have read and approved the final manuscript for publication.

## Acknowledgements

This work was supported by a research grant from the SSAI Acta and the Anna Lisa and Sven Erik Lundgren's Foundations. The authors thank Ms. Nuray Güner, statistician, Region Skåne Kompetens Centrum, for statistical advice.

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**Table 1. Characteristics of the study population**

<b>Population Characteristics</b>	
<b>Number of patients</b>	51
<b>Gender (M/F)</b>	35/16
<b>Age at inclusion (yrs)</b>	66(57:76)
<b>BMI (kg/m<sup>2</sup>)</b>	25.8(23.4:28.9)
<b>Proportion with sepsis (%)</b>	67
<b>ICU mortality (%)</b>	29
<b>6-month mortality (%)</b>	37
<b>Proportion with ALI (%)*</b>	35
<b>Proportion with ARDS (%)*</b>	29
<b>Proportion with severe lung injury (%)+</b>	18
<b>APACHE II</b>	24(19:29)
<b>SOFA</b>	12(9:14)
<b>PaO<sub>2</sub>/FiO<sub>2</sub></b>	230(160:290)
<b>PEEP (mmHg)</b>	7(5:10)
<b>Arterial blood lactate (mmol/L)</b>	3.0(1.9:4.5)
<b>CI (L/min/m<sup>2</sup>)</b>	3.5(2.8:4.5)
<b>ITBVI (mL/m<sup>2</sup>)</b>	1010(840:1200)
<b>EVLW/PBW (mL/kg)</b>	9.7(7.7:12.4)
<b>EVLW/ABW (mL/kg)</b>	8.3(6.3:10.6)
<b>EVLW/PBV</b>	1.8(1.4:2.2)

\* as defined by the NAEECC (20), + as defined by Murray's lung injury score (21).

ABW: actual body weight; ALI: acute lung injury; APACHE II: Acute Physiology and Chronic Health Evaluation II Score; ARDS: acute respiratory distress syndrome; BMI: body mass index; CI: Cardiac Index; EVLW: Extravascular lung water; ICU: intensive care unit; ITBVI: Intrathoracic blood volume index; PBV: pulmonary blood volume; PBW: predicted body weight; PEEP: Positive End Expiratory Pressure; SOFA: Sequential Organ Failure Score.

**Table 2. Positive and negative likelihood ratios (LR+ and LR-), pre- and post-test odds for mortality given a positive EVLW test**

	EVLW alone			Combined with ALI			Combined with ARDS			Combined sLI					
	LR+	LR-	Pre-test odds	LR+	LR-	Pre-test odds	LR+	LR-	Pre-test odds	LR+	LR-	Pre-test odds	LR+	LR-	Pre-test odds
<b>EVLW/ABW</b>	1.83	0.55	0.38	2.27	0.70	0.38	1.89	0.79	0.38	4.40	0.70	0.38	4.40	0.70	0.38
<b>EVLW/PBW</b>	1.41	0.72	0.38	1.51	0.88	0.38	1.76	0.85	0.38	1.98	0.88	0.38	1.98	0.88	0.38
<b>EVLW/PBV</b>	2.11	0.59	0.38	1.76	0.85	0.38	2.11	0.86	0.38	3.52	0.78	0.38	3.52	0.78	0.38

A positive EVLW test is defined as EVLW/ABW > 10 ml/kg, EVLW/PBW > 10 ml/kg and EVLW/PBV > 1.5.

**Table 3. Sensitivity (Sens), specificity (Spec), positive and negative likelihood ratios (LR+ and LR-) of EVLW/ABW, EVLW/PBW and EVLW/PBV for a diagnosis of ALI, ARDS or severe lung injury (sLI)**

		<b>ALI</b>	<b>ARDS</b>	<b>sLI</b>
<b>EVLW/ABW</b>	Sens	0.50	0.53	0.44
	Spec	0.85	0.83	0.76
	LR+	3.30	3.2	1.87
	LR-	0.60	0.56	0.73
	Pre-test odds	0.55	0.42	0.21
	Post-test odds +	1.80	1.33	0.40
	Post-test odds -	0.32	0.23	0.16
<b>EVLW/PBW</b>	Sens	0.61	0.60	0.67
	Spec	0.70	0.67	0.81
	LR+	2.02	1.80	3.50
	LR-	0.56	0.60	0.41
	Pre-test odds	0.56	0.42	0.21
	Post-test odds +	1.10	0.75	0.75
	Post-test odds -	0.30	0.25	0.09
<b>EVLW/PBV</b>	Sens	0.89	0.87	1.0
	Spec	0.52	0.47	0.88
	LR+	1.83	1.64	8.4
	LR-	0.22	0.28	0
	Pre-test odds	0.55	0.42	0.21
	Post-test odds +	1.00	0.68	1.79
	Post-test odds -	0.12	0.12	0

Post-test odds given a positive (Post-test odds +) or negative EVLW test (Post-test odds -) are also shown. A positive EVLW test is defined as EVLW/ABW>10 ml/kg, EVLW/PBW>10 ml/kg and EVLW/PBV>1.5.

## Figure legends

### Figure 1. EVLW indexed to ABW and PBW in patients with and without ALI / ARDS.

(a) EVLW indexed to ABW and PBW in patients with and without ALI. Filled boxes = patients with ALI, unfilled boxes = patients without ALI; (10.4(7.4:16.7) vs 7.8(5.9:9.6),  $p=0.01$  for ABW; 12.4(9.4:17.7) vs 8.2(7.5:10.9),  $p=0.01$  for PBW). (b) EVLW indexed to ABW and PBW in patients with and without ARDS. Filled boxes = patients with ARDS, unfilled boxes = patients without ARDS; (10.0(8.4:16.7) vs 7.8(5.9:9.6),  $p=0.01$  for ABW; 12.4(9.4:17.7) vs 8.3(7.5:10.9),  $p=0.01$  for PBW).

\* denotes  $p<0.05$

### Figure 2. EVLW indexed to PBV in patients with and without ALI / ARDS.

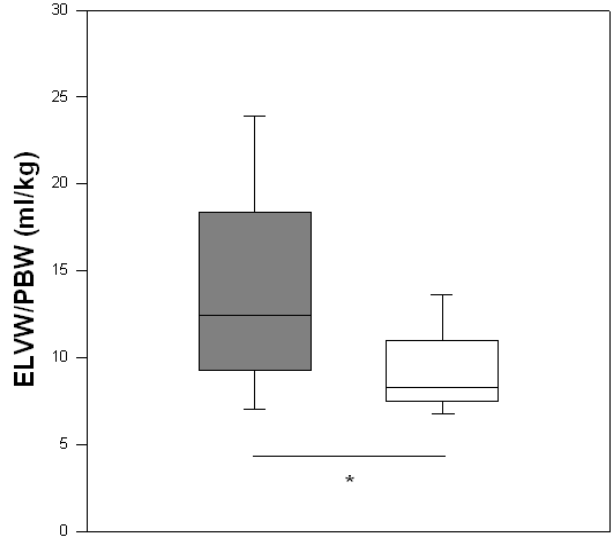
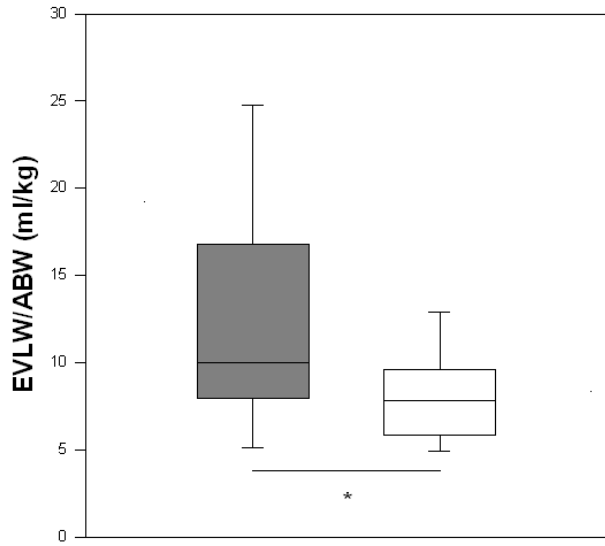
(a) EVLW indexed to PBV in patients with and without ALI. Filled boxes = patients with ALI, unfilled boxes = patients without ALI; (2.1(1.6:3.0) vs 1.6(1.3:1.9),  $p=0.02$  for PBV). (b) EVLW indexed to PBV in patients with and without ARDS. Filled boxes = patients with ARDS, unfilled boxes = patients without ARDS; (2.3(1.6:3.1) vs 1.7(1.3:1.9);  $p=0.04$  for PBV).

\* denotes  $p<0.05$

**Figure 3. Box plots for EVLW stratified by LIS.** \* =  $p<0.05$  and \*\* =  $p<0.01$ . Since there were only two patients in the group with LIS >3, it was omitted from statistical analyses and data is not shown.

**Figure 4. EVLW and mortality.** Filled bars = nonsurvivors, unfilled bars = survivors. \* denotes  $p<0.05$

### a) ALI



### b) ARDS

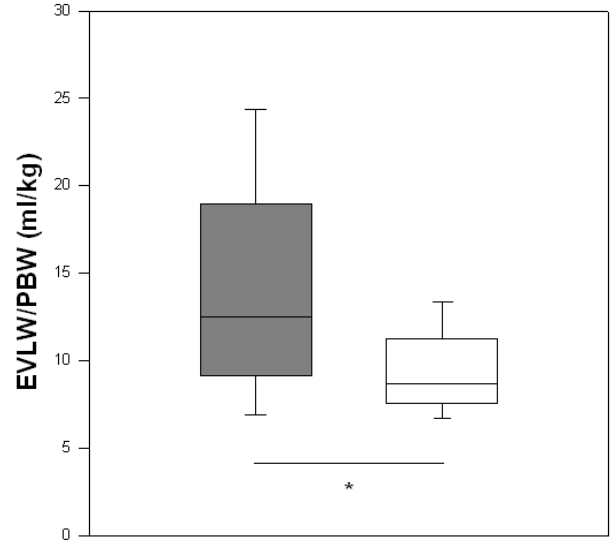
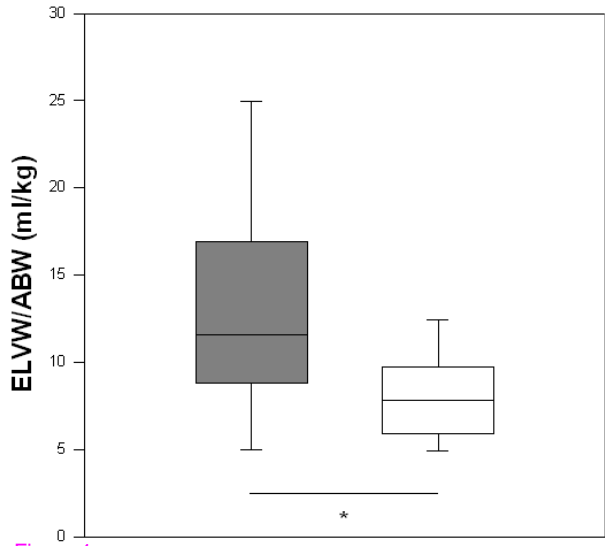
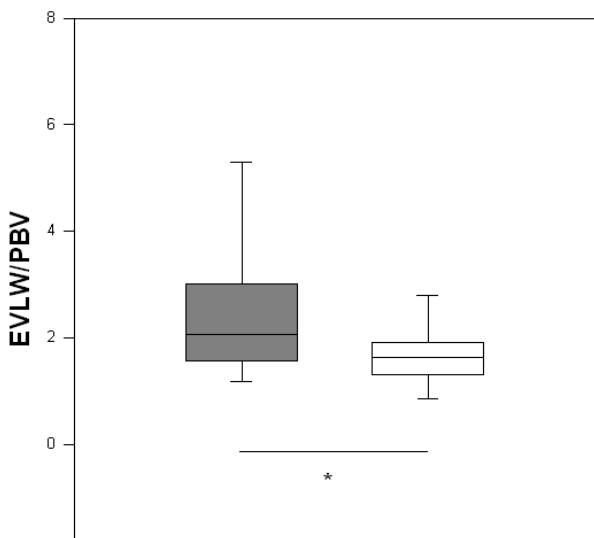


Figure 1

### a) ALI



### b) ARDS

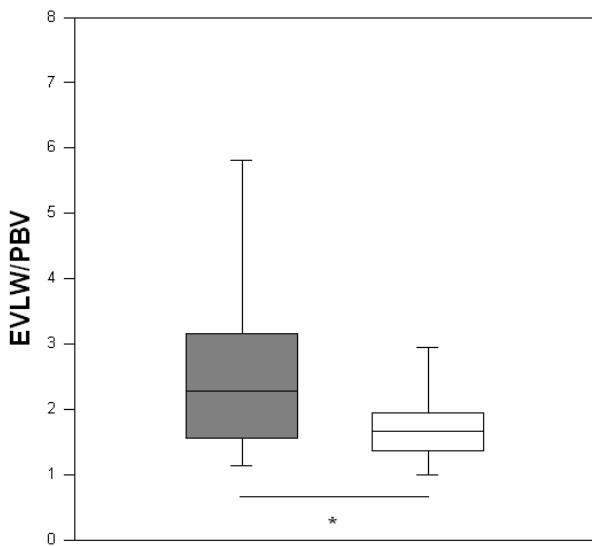


Figure 2

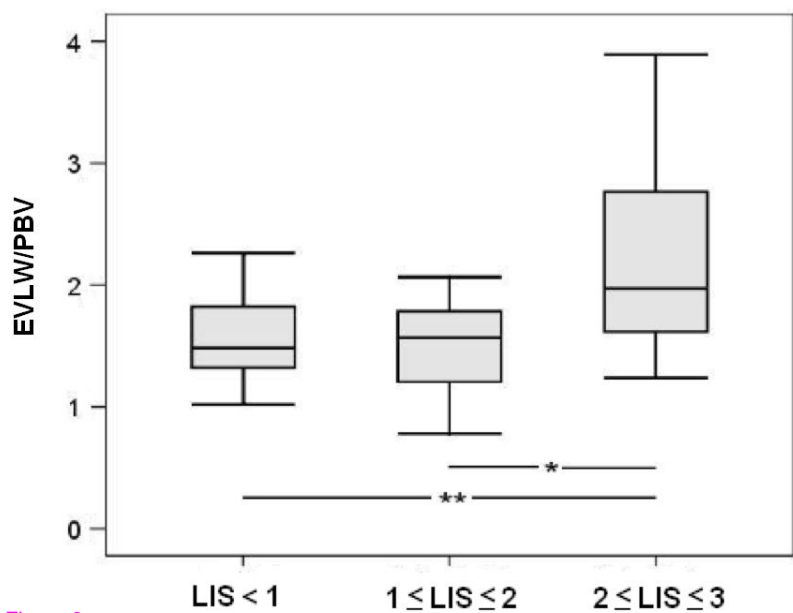
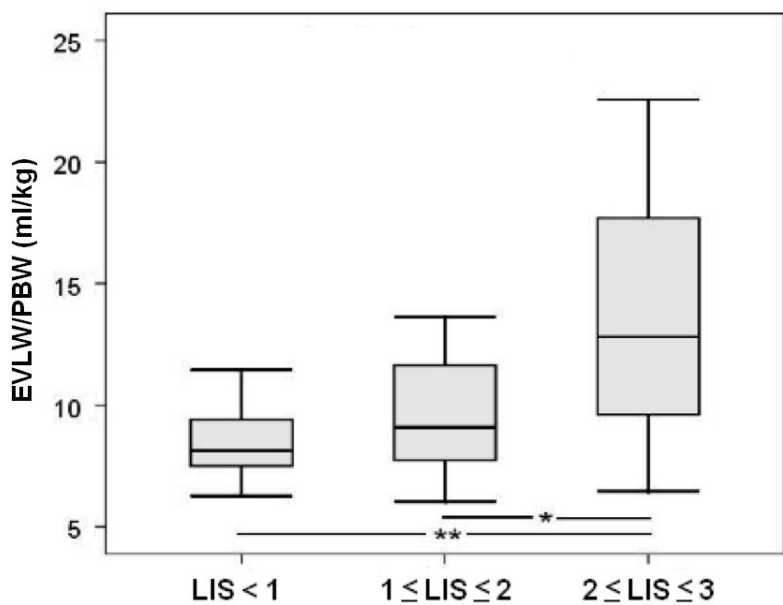
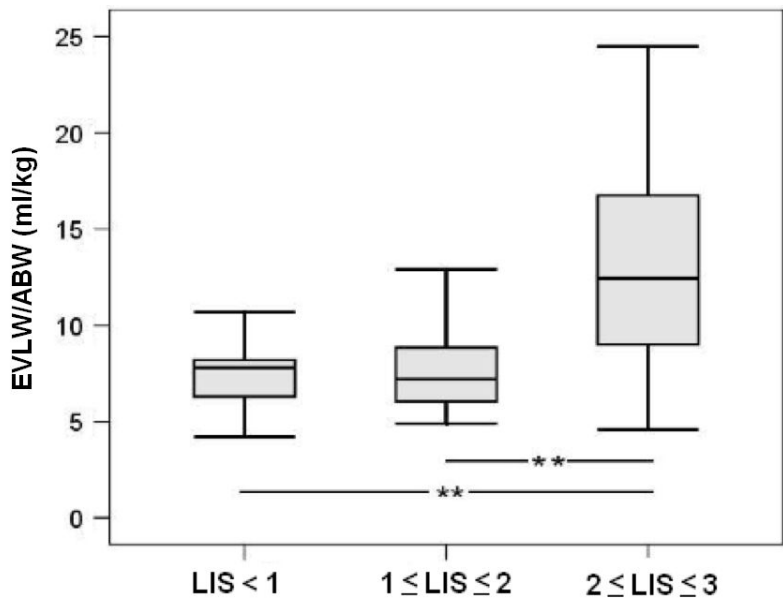


Figure 3

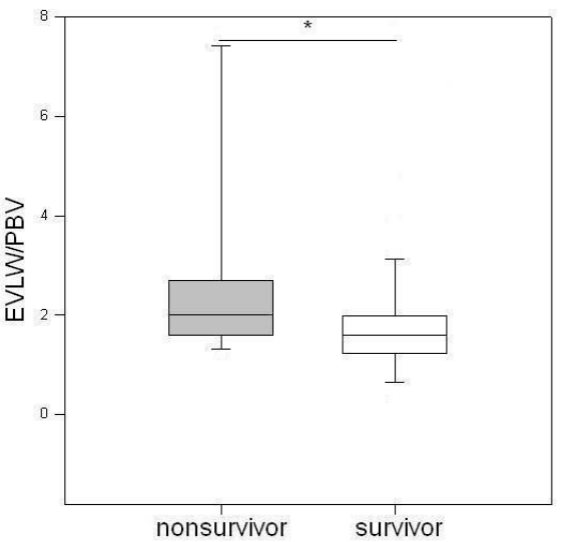
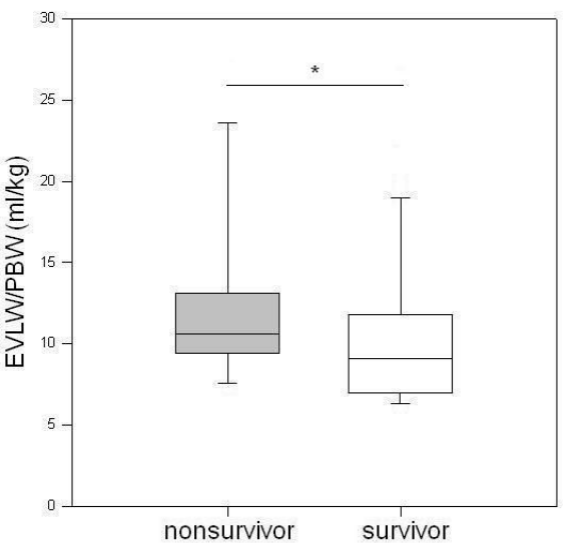
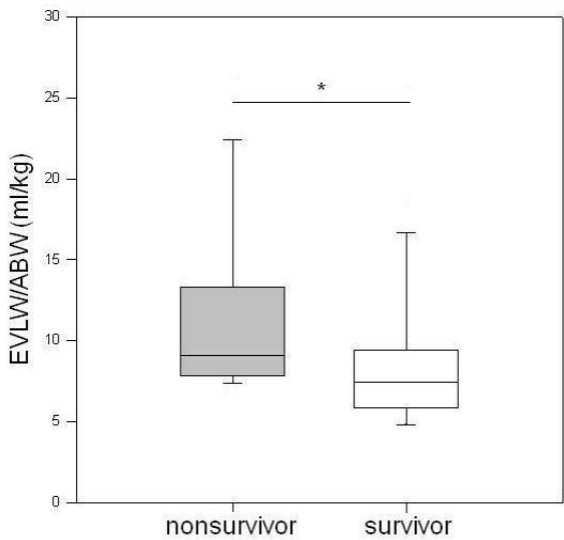


Figure 4