

constant during the study.

Results. EVLWI was significantly higher in ALI patients group compared to non-ALI patients group. In patients with ALI group 11/22 patients died (50%), in the non-ALI patients group 6/26 patients died (23%). EVLWI was significantly higher in patients that died compared to ones who survived.

Conclusion. EVLWI is a good indicator of early acute lung injury in surgical patients with sepsis.

Key words: extravascular lung water index, acute lung injury, PiCCO monitoring, sepsis

Introduction

It is possible to measure EVLWI (ExtraVascular Lung Water Index) by TPTD (TransPulmonary ThermoDilution) technique using PiCCO (Pulse-induced Contour Cardiac Output) monitoring. It is a standard minimally invasive method used for continuous monitoring of haemodynamic and volumetric parameters combining TPTD method and pulse curve analysis. (1,2)

EVLWI is defined as the difference between ITTV (IntraThoracic Thermal Volume), which is measured by transpulmonary thermodilution, and ITBV (IntraThoracic Blood Volume), see formula 1. By indexing the retrieved data according to body mass we can extrapolate EVLWI, see formula 2. As it is not possible to get ITBV by transpulmonary thermodilution, instead an indirect indicator is measured, that is GEDV (Global End-Diastolic Volume), see formula 3. EVLWI is indicative of the volume in interstitial lung tissue and intraalveolar space. (3,4) Indirect acute lung injury is a common consequence of sepsis. According to the literature, Acute Lung Injury (ALI) occurs in 37-41% of all sepsis patients. Depending on the diagnostic criteria, age groups and therapeutic protocols, the death rate is 29-42%. (5-12) ALI is characterized by hypoxemia, non-cardiogenic lung oedema, poor lung compliance and increased alveolar capillary permeability. (13)

Increased alveolar capillary permeability is a result of bacterial endotoxins, migration and adherence of polymorphonuclear leukocytes as well as a number of inflammatory factors: neutrophil elastase, collagenase A and B, protease and nitric oxide. Other pro-inflammatory factors transmit the systemic inflammatory response to the lungs: TNF- α (tumour necrosis factor α), IL-1 β (interleukin 1 β), IL-

6 (interleukin 6), IL-8 (interleukin 8), leukotriene and cyclooxygenase pathways without fibrinolysis, the C5a complement system, along with numerous chemokines and cytokines. (14)

Along with the aforementioned, the intensity of alveolar injury is dependent on the activity of thrombin, oxygen radicals, proteolytic enzymes and adhesion molecules. As a result surfactant formation is insufficient and its action is inadequate. Consequently, destruction of capillary endothelium and alveolar epithelium causes increased vascular permeability and quickly results in fluid collection in the interstitial space and in alveoli. (14)

The EVLWI reference range in healthy adults is 3.0-7.0ml/kg. EVLWI values above 10ml/kg indicate development of pulmonary oedema and correlate with morbidity and mortality. A 100% increase in EVLWI values are not clinically evident on chest x-rays, while those of a 200-300% increase are correlated to significant hypoxemia. (15)

The goal of this paper is to examine the correlation and dynamics of the EVLWI as an indicator of acute lung injury in septic patients who have undergone major abdominal surgery.

Materials and methods

This prospective observational study was conducted from May 2009 until October 2011, at the Department of Anaesthesiology, Reanimatology and Intensive care at the University Hospital of Zagreb. It included 48 septic patients who had undergone major abdominal surgery. Of the 48 patients, 25 were male aged 47 (SD=8) and 23 were female aged 43 (SD=7). They were divided into two groups. The first consisted of 22 patients who had ALI (ALI patients group), the second group, consisted of 26 patients, who were without ALI (non-ALI patients group). All of the participants had signed informed consent.

Diagnosis of both sepsis and ALI was based upon internationally defined criteria, clinical signs and symptoms, as well as laboratory results. (16-20)

Exclusion criteria are listed in table 1.

Upon admission to the intensive care unit, post-operatively, all of the patients had endotracheal tubes and were mechanically ventilated. They were all

analgo-sedated with midazolam (0.08–0.2mg/kg/h) and sufentanil (0.3–0.5µg/kg). Both drugs were applied intravenously by a syringe pump system.

Patients who were haemodynamically unstable (mean arterial pressure < 60mmHg) were given vasoactive drugs (norepinephrine 0.6–1.8µg/kg/min), and had their SOFA (Sequential Organ Failure Assessment) score calculated.

The ventilation mode was BIPAP (BiPhasic Positive Airway Pressure) and was set to FiO₂ (fraction of inspired oxygen) 0.4–0.8, respiratory rate of 12–18/min, P_{high} (pressure high) 15–25cmH₂O, P_{low} (pressure low) 5–8cmH₂O, T_{high} (time high) 2–5s, T_{low} (time low) 0.5–1.0s. All patients had a dual-lumen central venous catheter (Arrow International, 7F, 20cm, Athlone, Ireland) placed in the internal jugular vein. Each patient had a chest x-ray done in order to confirm that the catheter was in place. Next, an intraarterial PiCCO catheter (PulsioCath PV2014L16N, 4F) was placed into the femoral artery using Seldinger's method. Primary monitor used was Dräger Infinity Delta XL, Germany, with secondary input from PiCCO Dräger Infinity R PiCCO Smart Pod TM.

All of the measured variables, EVLWI, GEDVI (Global End-Diastolic Volume Index), ITBVI, CI (Cardiac Index) and SVRI (Systemic Vascular Resistance Index) were taken in both study groups using PiCCO in the same 8-hour intervals, three times a day throughout the study.

Each measurement was done using a thermodilution indicator, 15ml of cold (<8°C) 5% glucose solution, which was injected through the central venous catheter. The final value was the mean of three consecutive measurements, each taken within 5-minute intervals. PiCCO monitoring was used in both study groups within a seven-day time period until they achieved optimal haemodynamic and TPTD values. During this time period HR (Heart Rate), MAP (Mean Arterial Pressure), serum albumin concentration (as an indirect indicator of oncotic pressure within vascular system), PaCO₂ (arterial partial pressure of carbon dioxide), PaO₂ (arterial partial pressure of oxygen), PaO₂/FiO₂ ratio (arterial partial pressure of oxygen/fraction of inspired oxygen), lung compliance and resistance, ScvO₂ (central venous oxygen saturation) were all regularly measured.

Both study groups had chest x-rays, ECGs and transthoracic heart ultrasound (Siemens P4-2 probe) done in order to measure their left ventricular ejection fraction and diastolic heart dysfunction.

Both groups of patients were given crystalloids (30ml/kg) up to the point at which

their optimal preload was achieved (MAP>60mmHg, EVLWI<7ml/kg, ITBVI 850-1000ml/m², GEDVI 680-800ml/m²). Patients with haemoglobin concentration <70g/l and/or CI≤2.5l/min/m² were given packed red cell transfusion.

All of the data measured or calculated was statistically processed using the independent t-test, along with ANOVA (ANalysis Of VAriance) applied for repeating measurements. Values of p<0.05 were considered statistically significant.

Results

The study included 48 septic patients who had undergone major abdominal surgery. Of those, 22 had ALI and 26 did not. There were 14 male and 8 female patients in ALI group versus 11 male and 15 female patients in non-ALI group. Table 2 displays the results according to age, APACHE II (Acute Physiology and Chronic Health Evaluation II) score and SOFA score in ALI and non-ALI group. Patients with positive haemocultures received antibiotics according to the antibiogram (table 3). Microorganisms isolated from bronchoalveolar lavage samples in patients with ALI group are displayed in table 4.

EVLWI was markedly increased in the ALI patient group between the 3rd and 7th day. Also, a statistically significant difference in EVLWI values was found between the two groups within the 1st and 7th day (table 5). Furthermore, there was an evident positive growth trend of EVLWI with each passing day (table 5).

Figure 1 depicts the trends and differences of EVLWI in the two groups over a period of seven days. There is a discrepancy between the median of EVLWI in the two groups from 4th to 7th day. That is, the EVLWI in the non-ALI group of patients reaches a plateau, while in the ALI group it continues to rise.

Figure 2 depicts AUROC (Area Under Receiver Operating Characteristic) curve for EVLWI (0.943; 95% confidence interval 0.849-0.987) with p<0.001.

Optimal discrimination threshold between the groups was 14% for EVLWI (sensitivity 72.2%, specificity 97.5%) which indicates that this diagnostic method is efficient.

There was also a statistically significant difference throughout the rest of the values measured in both groups: GEDVI, ITBVI, SVRI and CVP. Mean values of

GEDVI as well as ITBVI in ALI group of patients were higher than reference values (table 6). CI values did not show a statistically significant difference between the two groups (table 6).

In the ALI patient group, there was a sharp rise in PaCO₂ from the 3rd day, while the non-ALI patient group showed a trend towards a decrease in PaCO₂ from the 1st day onwards (table 5, figure 3). On the other hand, the measured difference in PaO₂ in both patient groups showed a constant drop in PaO₂ in the ALI patient group during a week-long observation that was greater than the decrease in PaO₂ in the non-ALI patient group (table 5, figure 4). Albumin values were also tracked during the seven-day period. The results show that serum albumin concentration in the non-ALI patient group was greater in comparison to ALI patient group (table 5, figure 5). Patients with ALI had increased EVLWI values and reduced serum albumin concentrations.

The following lung function indices were monitored: PaO₂/FiO₂ ratio, compliance, lung resistance and LIS (Lung Injury Score). The ALI patient group had a significantly higher resistance of the respiratory system and reduced compliance and PaO₂/FiO₂ ratio in comparison to non-ALI patient group (table 7).

Total seven-day mortality in both research groups was 17/48 patients (35%). In the ALI patient group 11/22 patients died (50%), while 6/26 (23%) patients died in the non-ALI patient group. Measured EVLWI values on the 7th day of monitoring were significantly increased in the group of deceased patients in comparison to those who survived: 16.5ml/kg vs 12.4ml/kg (figure 6).

Discussion

The results of this research study show that the EVLWI can be used in the assessment of the appearance and dynamics of acute lung injury in surgical patients with sepsis.

This is shown in the significantly higher EVLWI values in the ALI patient group when compared to the non-ALI patient group. EVLWI values in the ALI patient group were higher in patients who died than in those who survived. The initially measured EVLWI values in the ALI patient group were higher than in the non-ALI patient group, however it was still within the reference interval spread. A significant increase in measured EVLWI values in the ALI patient group began on

the 3rd day and maximum values were attained on the 7th day of measurement. Simultaneously with the increase in EVLWI, the ALI patient group presented a reduced serum albumin concentration. In the ALI patient group an increase in EVLWI resulted in significant lung function disorder, which could be seen through changes in relations between PaO₂/FiO₂ ratio, lung compliance and lung resistance. The resulting hypoxemia was the result of hindered oxygen diffusion through the alveocapillary membrane and reduced lung compliance as well as increased lung resistance that stemmed from oedema and lung collapse.

The measured EVLWI values and the dynamics of the increase in the ALI patient group is in accordance with the stated goal of this research, as well as with the current knowledge on the subject. Recent data from the literature supports the effectiveness of EVLWI as an indicator for early detection of patients with ALI. (21, 22)

Cordemans et al. confirm the significance of the connection between EVLWI dynamics, intraabdominal hypertension, preload optimisation with fluid therapy in mechanically ventilated patients and poor treatment results in patients with ALI. (23) The meta-analysis of Zhongheng et al investigated EVLWI as an indicator of poor outcome in non-surgical patients with burns, sepsis and ALI. It included 11 studies carried out in 9 countries with a total of 670 patients between 1999 and 2010. EVLWI was significantly increased in the group of deceased patients in comparison to those who survived, with a median of 5.06ml/kg. (24) Our research showed a median of 6.6ml/kg.

The meta-regression analysis carried out by Eichhorn et al. researched the connection between EVLWI and GEDVI in the optimisation of preload in two different patient groups with sepsis, surgical and non-surgical. The surgical group consisted of patients after cardiac surgery, neurosurgery and vascular surgery. It analyzed a total of 138 studies with a total of 4682 patients published on PubMed with the keywords EVLWI, GEDVI and TPTD between 1990 and 2010. EVLWI and GEDVI were significantly higher in the patient group with sepsis after major surgery. (25)

Maharaj's overview consisted of research of PubMed using EVLWI, ALI and ARDS (Acute Respiratory Distress Syndrome) as keywords. It examined the usefulness of exact EVLWI quantification in diagnosis, treatment and prognosis of both ALI and ARDS.

In conclusion, EVLWI is a useful indicator of clinical behaviour in mechanically ventilated patients, especially during PEEP (Positive End-Expiratory Pressure) titration, optimisation of volume therapy and poor patient outcome. (26)

The level of PEEP applied during mechanical ventilation can influence the measured EVLWI values, therefore the ventilator settings were constant throughout the research period. Of course, as in all research, this study has drawbacks: specifics of the observed population – surgical patients after laparotomy. Furthermore, the reliability of EVLWI measurements is reduced through vascular lung obstruction along with a change in the ventilation/perfusion ratio, including hypoxic lung vasoconstriction and a high PEEP level. An additional drawback is a small patient sample included in the research. Finally, the usefulness of applying TPTD technology in patients with heart shunts (recirculation of the indicator) is questionable. Both the first and the second group represented critically ill patients in need of haemodynamic monitoring that is minimally invasive, with a goal of preventing possible complications.

The results of this research show that EVLWI can be useful for early detection of patients with ALI.

This is in accordance with expectations and assumptions built upon current literature. Insofar as all standards and prerequisites for the application of PiCCO monitors have been met, the obtained data on EVLWI make it a good indicator of the early onset of acute lung injury in patients with sepsis. EVLWI can also be an indicator of the effectiveness of the therapy in treating ALI, especially fluid therapy, mechanical ventilation strategies and treatment outcomes. However, for definitive confirmation of EVLWI value in an assessment of the onset of acute lung injury in patients with sepsis after major abdominal surgery, further research on a larger number of patients is necessary.

Formula 1.

$$EVLW = ITTV - ITBV$$

EVLW, ExtraVascular Lung Water; ITBV, IntraThoracic Blood Volume; ITTV, IntraThoracic Thermal Volume.

Formula 2.

$$EVLWI = EVLW / (\text{predicted body weight})$$

EVLW, ExtraVascular Lung Water; EVLWI, ExtraVascular Lung Water Index.

Formula 3.

$$ITBV=1.25 \times GEDV - 28.4$$

GEDV, Global End-Diastolic Volume; ITBV, IntraThoracic Blood Volume.

Table 1. Exclusion criteria.

EXCLUSION CRITERIA
Coagulation disorders
Cardiomyopathy
Aortic valve insufficiency
Left ventricular ejection fraction <45%
Chronic obstructive lung disease
Children
Pregnant women
Patients who did not sign informed consent
Patients with contraindication for femoral artery puncture
Allergic diathesis
Disseminated malignancy

Table 2. Results according to age, APACHE II score and SOFA score in ALI patients group and non-ALI patients group. Data were statistically analyzed using independent t-test.

Property	Mean	SD	t	P
Age	non-ALI	42.88	7.14	0.181
	ALI	40.52	7.1	
APACHE II score	non-ALI	24.22	4.3	<0.001
	ALI	27.02	7.7	
SOFA score	non-ALI	9.6	0.8-18.3	<0.001
	ALI	13.1	0.7	

ALI, Acute Lung Injury; APACHE II, Acute Physiology and Chronic Health Evaluation II score; SOFA score, Sequential Organ Failure Assessment score.

Table 3. Microorganisms isolated from haemocultures of ALI patients group and non-ALI patients group and their respective antibiotic therapy.

Microorganism	Number of positive haemocultures		Antibiotic(s)
	Patients with ALIn(%)	Patients without ALIn(%)	
S. aureus	2(6.9)	3(15.8)	cloxacillin, clindamycin
S. aureus (MRSA)	6(20.7)	4(21.1)	teicoplanin, vancomycin
Coagulase negative staphylococcus	4(13.8)	2(10.5)	teicoplanin, vancomycin
P. aeruginosa	8(27.6)	6(31.6)	meropenem, colistin
K. pneumoniae ESBL	5(17.2)	2(10.5)	meropenem, cefepime
A. baumannii	4(13.8)	2(10.5)	meropenem

ALI, Acute Lung Injury; ESBL, Extended Spectrum Beta Lactamase; MRSA, Methicillin Resistant Staphylococcus Aureus.

Table 4. Microorganisms isolated from bronchoalveolar lavage samples in ALI patient group.

Microorganism	Number of positive culturesn(%)
S. aureus (MRSA)	4(18.2)
P. aeruginosa	6(27.3)
K. pneumoniae ESBL	3(13.6)
C. albicans	5(22.7)
C. dubliniensis	1(4.5)
C. krusei	3(13.6)

ALI, Acute Lung Injury; ESBL, Extended Spectrum Beta Lactamase; MRSA, Methicillin Resistant Staphylococcus Aureus

Table 5. Transpulmonary thermodilution and laboratories data in ALI patient group and non-ALI patient group during the seven-day period. Data were statistically analyzed using independent t-test.

Variable	Time ALIn=22non-ALIn=26t		P
	Mean	SD	
EVLWI(ml/kg)Day	17.09	0.29	5.27 0.35 19.37 <0.001

	Day 27.64	0.23	6.19	0.35	16.48	<0.001
	Day 38.00	0.35	6.71	0.25	15.00	<0.001
	Day 411.85	0.53	6.91	0.17	45.31	<0.001
	Day 513.53	0.71	7.35	0.25	41.62	<0.001
	Day 614.42	0.79	7.76	0.24	40.82	<0.001
	Day 715.30	0.95	7.93	0.25	38.15	<0.001
Albumin(g/L)	Day 117.11	3.73	44.92	2.98	-28.71	<0.001
	Day 215.88	3.16	44.09	2.65	-33.67	<0.001
	Day 315.19	2.77	43.59	2.73	-35.67	<0.001
	Day 414.64	2.55	43.36	2.71	-37.56	<0.001
	Day 514.42	2.18	43.19	2.57	-41.36	<0.001
	Day 614.46	2.14	42.82	2.61	-40.60	<0.001
	Day 714.61	2.27	42.48	2.66	-38.62	<0.001
PaCO ₂ (kPa)	Day 15.37	0.50	5.95	0.50	-4.01	<0.001
	Day 25.43	0.70	5.64	0.50	-1.21	0.231
	Day 35.56	0.80	5.47	0.50	0.47	0.638
	Day 46.06	0.86	5.35	0.47	3.62	0.001
	Day 56.54	1.03	5.16	0.54	5.94	<0.001
	Day 66.75	1.18	5.16	0.55	6.17	<0.001
	Day 77.05	1.42	5.11	0.47	6.56	<0.001
PaO ₂ (kPa)	Day 117.40	5.13	30.68	1.83	-12.34	<0.001
	Day 215.58	5.03	27.64	2.78	-10.50	<0.001
	Day 314.23	5.46	24.53	3.87	-7.62	<0.001
	Day 413.04	3.53	21.90	4.18	-7.85	<0.001
	Day 511.93	2.00	19.50	4.40	-7.44	<0.001
	Day 611.23	1.34	17.97	4.27	-7.09	<0.001
	Day 710.87	1.76	16.33	4.01	-5.91	<0.001

ALI, Acute Lung Injury; EVLWI, ExtraVascular Lung Water Index; P, significance level; PaCO₂, arterial partial pressure of carbon dioxide; PaO₂, arterial partial pressure of oxygen; t, t score for independent t-test.

Table 6. Haemodynamic data in ALI patient group and non-ALI patient group during the seven-day period. Data were statistically analyzed using independent t-test.

GEDVI(ml/m²) ITBVI(ml/m²) CI(L/min/m²) SVRI(dyn×s×cm²/m²) ScvO₂(%) CVP(mmHg)

Reference values	680-800	850-1000	3.0-5.0	1700-2400	65-75	0-8	
non-ALI n=26	Mean±SD	697.0±55.1	907.5±65.3	4.2±0.4	2050.0±185.8	73.9±2.8	9.5±0.9
ALI n=22	Day 1 mean ±SD	947.0±214.0	1087.0±245.8	4.0±1.2	1530.1±530.7	72.6±6.3	10.3±1.6
	Test results*	t=5.7p<0.001	t=3.6p<0.001	t=-0.8p=0.428	t=-4.7p<0.001	t=-0.9p=0.347	t=2.2p=0.035
	Day 2 mean ±SD	988.8±194.5	1120.7±232.6	4.2±1.1	1497.1±423.1	73.2±7.7	10.1±1.5
	Test results*	t=7.3p<0.001	t=4.5p<0.001	t=0.0p=0.999	t=-0.6p<0.001	t=-0.4p=0.668	t=1.7p=0.094
	Day 3 mean ±SD	1026.3±179.4	1165.7±222.1	4.3±1.1	1506.3±347.1	73.6±7.4	12.1±1.4
	Test results*	t=8.9p<0.001	t=5.7p<0.001	t=0.4p=0.668	t=-6.9p<0.001	t=-0.2p=0.849	t=7.7p<0.001
	Day 4 mean ±SD	1053.9±164.1	1196.1±218.3	4.4±1.2	1469.4±325.2	77.4±5.9	11.8±1.4
	Test results*	t=10.4p<0.001	t=6.4p<0.001	t=0.8p=0.427	t=-7.7p<0.001	t=2.6p=0.009	t=6.8p<0.001
	Day 5 mean ±SD	1081.1±164.7	1213.8±218.5	4.4±1.2	1375.7±365.1	77.2±5.5	11.4±1.3
	Test results*	t=11.2p<0.001	t=6.8p<0.001	t=0.8p=0.427	t=-8.2p<0.001	t=2.6p=0.010	t=5.9p<0.001
	Day 6 mean ±SD	1093.7±176.1	1233.6±222.9	4.4±1.3	1323.0±443.3	76.8±7.1	11.6±1.6
	Test results*	t=10.9p<0.001	t=7.1p<0.001	t=0.7p=0.460	t=-7.6p<0.001	t=1.9p=0.061	t=5.7p<0.001
	Day 7 mean ±SD	1068.8±159.7	1181.8±186.4	4.5±1.1	1500.0±391.1	72.2±8.8	10.8±1.2
	Test results*	t=11.3p<0.001	t=7.0p<0.001	t=1.3p=0.201	t=-6.4p<0.001	t=-0.9p=0.356	t=4.3p<0.001

ALI, Acute Lung Injury; CI, Cardiac Index; CVP, Central Venous Pressure; GEDVI, Global End-Diastolic Volume Index; ITBVI, IntraThoracic Blood Volume Index; ScvO₂, central venous oxygen saturation; SVRI, Systemic Vascular Resistance Index.

*independent t-test results compared to non-ALI patients

Table 7. Lung function indicators expressed as a standard deviation in ALI patient group and non-ALI patient group. Data were statistically analyzed using independent t-test.

Variable	ALI n=22		non-ALI n=26		P
	Mean	SD	Mean	SD	

PaO ₂ /FiO ₂	19.33	0.75	42.77	1.16	-81.31	<0.001
Compliance(ml/cmH ₂ O)	13.56	0.62	22.19	1.43	-26.28	<0.001
Resistance(cmH ₂ O/L/s)	3.33	0.46	2.33	0.50	7.14	<0.001
LIS score	1.60	0.36	0.00	0.00	2.88	<0.001

ALI, Acute Lung Injury; LIS, Lung Injury severity Score; P, significance level; PaO₂/FiO₂, arterial pressure of oxygen/fraction of inspired oxygen; SD, standard deviation; t, t score for independent t-test.

Figure 1. EVLWI (ExtraVascular Lung Water Index) in ALI (Acute Lung Injury) patient group and non-ALI patient group during the seven-day period. Data were analyzed using independent t-test and ANOVA (ANalysis Of VAriance).

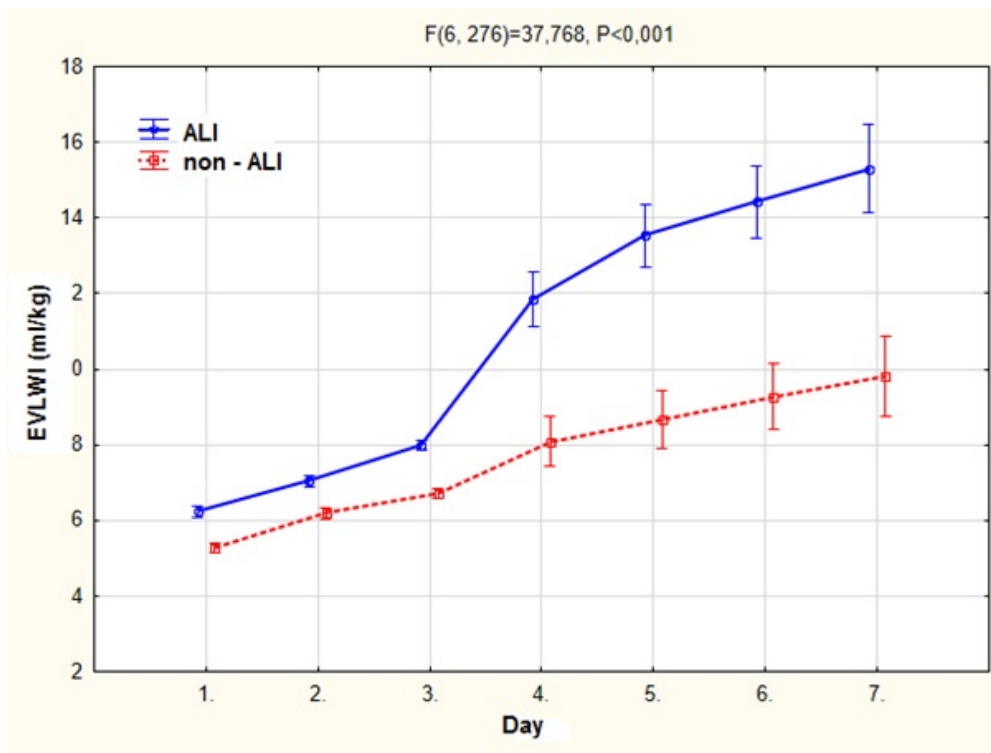


Figure 2. AUROC (Area Under Receiver Operating Characteristic) curve for EVLWI (ExtraVascular Lung Water Index); (0.943; 95% confidence interval 0.849-0.987) with p<0.001.

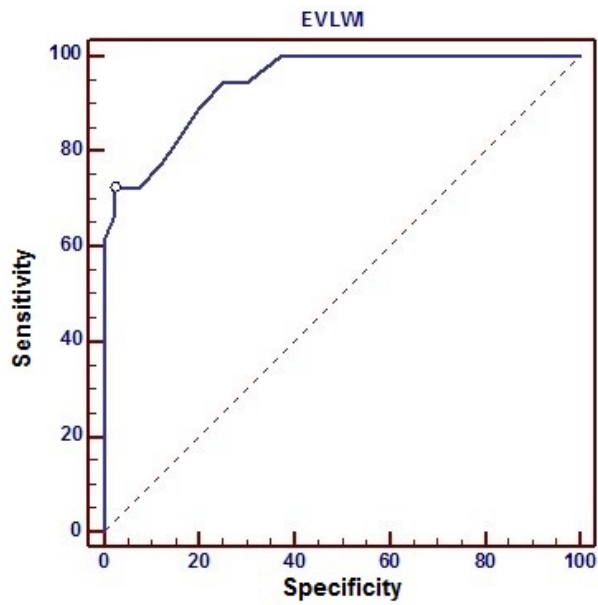


Figure 3. PaCO₂ (arterial partial pressure of carbon dioxide) in ALI (Acute Lung Injury) patient group and non-ALI patient group during the seven-day period. Data were analyzed using independent t-test and ANOVA (ANalysis Of VAriance).

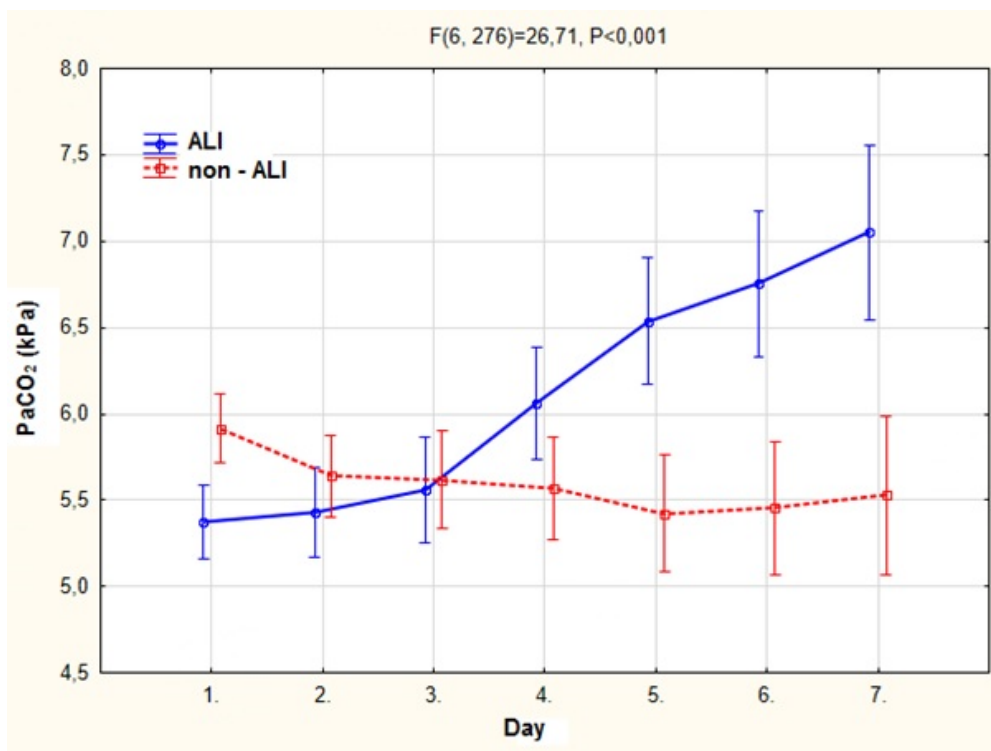


Figure 4. PaO₂ (arterial partial pressure of oxygen) in ALI (Acute Lung Injury) patient group and non-ALI patient group during the seven-day period. Data were analyzed using independent t-test and ANOVA (ANalysis Of VAriance).

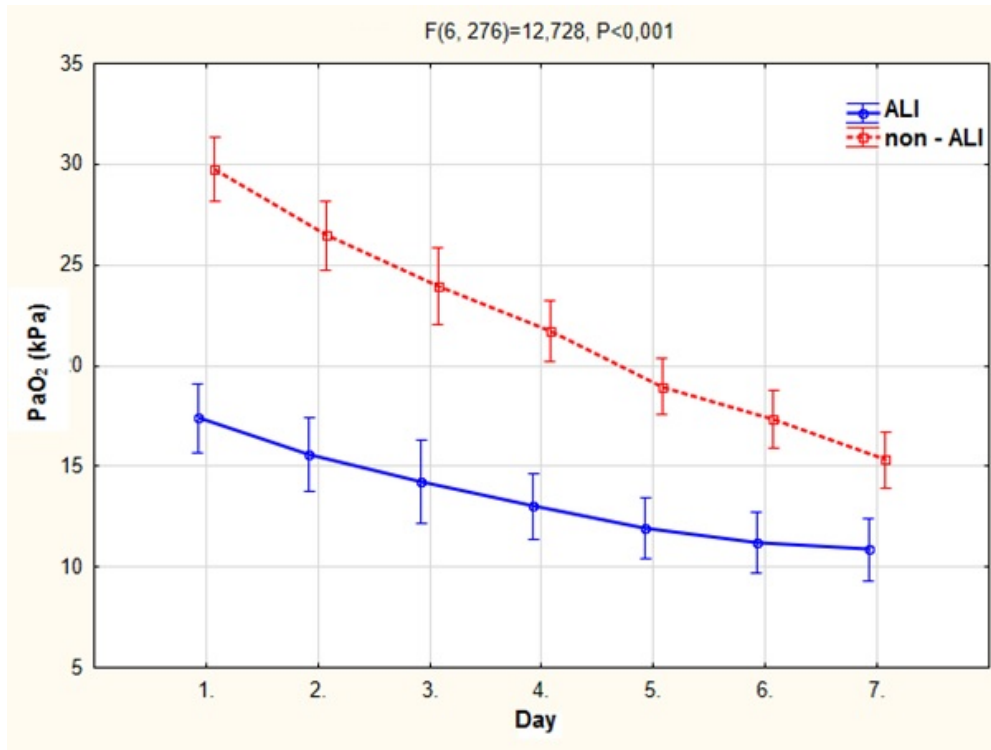


Figure 5. Serum albumin concentration in ALI (Acute Lung Injury) patient group and non-ALI patient group during the seven-day period. Data were analyzed using independent t-test and ANOVA (ANalysis Of VAriance).

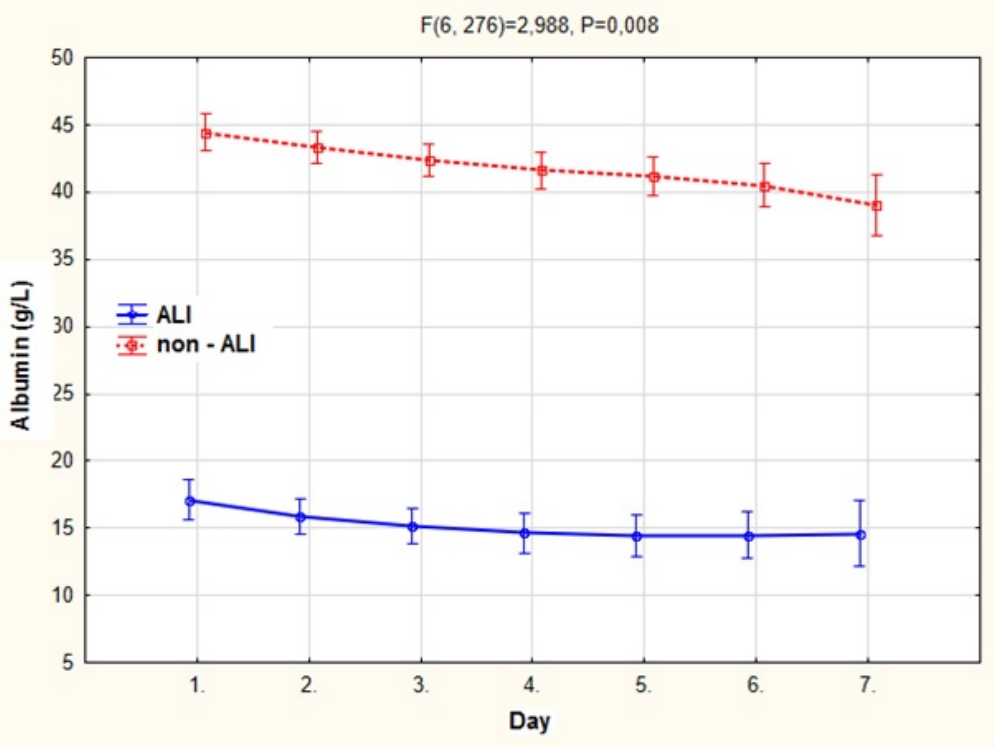
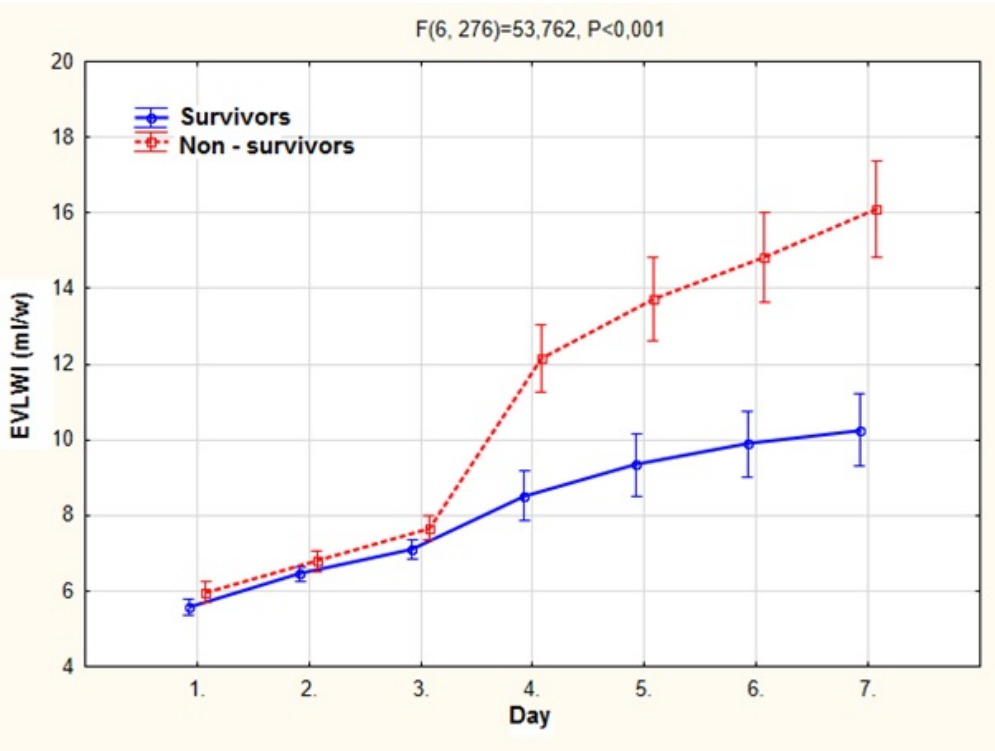


Figure 6. EVLWI (ExtraVascular Lung Water Index) in patients who survived and patients who did not survive sepsis after major abdominal surgery in this study. Data were analyzed using independent t-test and ANOVA (ANalysis Of VARIance).



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