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Combined Estimation of Serum Procalcitonin Levels and Clinical Pulmonary Infection Score Improves Predictability for Survival of Ventilation-associated Pneumonia Patients

Adel F. Al-Kholy[1]*, Ahmed E. Salem[2], Maha M. Hagras[3]

[1]Department of Medical Biochemistry, Faculty of Medicine, Benha University, Egypt
[2]Department of Anesthesia & ICU, Faculty of Medicine, Tanta University, Egypt
[3]Department of Clinical Pathology, Faculty of Medicine, Tanta University, Egypt

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Keywords

- Ventilator-associated pneumonia
- C-reactive protein
- Procacitonin
- CPIS score
- Survival rate

Abstract

Objectives: To evaluate predictability of estimation of C-reactive protein (CRP) and procalcitonin (PCT) levels for diagnosis and survival of ventilator-associated pneumonia (VAP) patients. **Patients & Methods**: The study included 53 VAP patients and 37 No VAP patients who were assessed using Clinical Pulmonary Infection Score (CPIS) and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores. Blood samples were collected on D0 and D4 for estimation of serum CRP and PCT levels. Patients were managed according to Surviving Sepsis Campaign guidelines. The 28-day mortality rate (MR) and the predictors for mortality were determined. **Results:** Total MR was 43.3% with significant difference between both groups. APACHE II and CPIS scores were significantly higher in non-survivors of both groups and in VAP than No VAP patients. Serum CRP and PCT levels were significantly higher in VAP patients and in non-survivors than survivors. Change of CRP level was significantly higher in No VAP than VAP survivors, while change of PCT levels was significantly higher in VAP survivors than non-survivors. High CPIS score and D0 PCT level, but low decreases of CRP and PCT levels are positive predictors for VAP diagnosis. High D4 PCT level and CPIS scores, but low decreases of PCT levels are significant predictors for mortality. **Conclusion**: VAP had high 28-day mortality rate. Combined evaluation of CPIS score and PCT levels improved the ability to diagnose VAP and low levels of both are independent predictors of survival.

Corresponding author: Adel F. Al-Kholy, Department of Medical Biochemistry, Faculty of Medicine, Benha University, e-mail: adeladel59@yahoo.com; 01222864679

Introduction

Ventilator-associated infection according to criteria from the Centers for Disease Control and Prevention include pneumonia, infection-related ventilator-associated condition, tracheobronchitis, and lower respiratory tract infection (1). However, ventilator-associated pneumonia (VAP) is the most common nosocomial infections in patients admitted to the ICU (2).

Diagnosis of VAP is mainly based on clinical presentation with a lung infection occurring after 48 hours of mechanical ventilation (MV) with a new infiltrate on chest X-ray (3). However, both current and modified ventilator-associated events criteria have poor sensitivity but good specificity in identifying VAP (4).

Procalcitonin (PCT), the precursor molecule of calcitonin, is produced by the C cells of the thyroid, but is devoid of known hormonal activity (5). Normally all PCT is cleaved intracellularly into calcitonin, katacalcin, and an N-terminal residue and in health, minute quantities are released into the blood stream (6). Synthesis of PCT is stimulated by inflammatory mediators and bacterial toxins (7), so its production is upregulated in bacterial infection (5).

Clinical studies failed to show a significant correlation between using the classic inflammatory biomarkers and infection-related mortality (8). Meta-analysis of published studies demonstrates that PCT is more specific and has better diagnostic accuracy than CRP for bacterial infection in systemic rheumatic diseases (9), end-stage renal disease (10) and end-stage liver disease (11).

The current study was designed to evaluate the diagnostic yield of sequential estimation of serum CRP and serum PCT levels for diagnosis of VAP and predictability for survival of patients admitted to surgical ICU

Materials & Methods

The current prospective comparative study was conducted since Jan 2015 till June 2016 at Surgical Intensive Care Unit (SICU) and Clinical Pathology Department at Tanta University Hospitals and Some private ICU centers; in conjunction with Medical Biochemistry Department, Benha University. The study protocol was approved by the Local Ethical Committee at Tanta and Benha Universities and by the responsible personnel at these private ICU centers. The nearest relatives of the enrolled patients signed written fully informed consents for participation of their relatives in the current study.

The study intended to include patients who were admitted to ICU for need of mechanical ventilation (MV) and developed clinical and/or radiologic manifestations suggestive of developing pneumonia 48 hours after initiation of MV. VAP was diagnosed clinically depending on the guidelines of the **American Thoracic Society** (12). Patients developed VAP were categorized as early (occurring within 4 days of MV) or late (occurring on the 5th day of MV) (12, 13). Patients on MV who developed a picture suggestive of VAP but did not fulfill the VAP diagnostic criteria were included as No VAP group.

Patients with pneumonia prior to or within 48-hr of MV, patients with Adult Respiratory Distress

Syndrome (ARDS), cavitary lung disease based on chest X-ray findings, primary or secondary lung cancer or lung cystic fibrosis were excluded from the study. Tuberculosis patients and patients with acquired, induced or congenital immunodeficiency, leukopenia <1000 cells/mm3, neutropenia <500 PN/mm3 were also excluded from the study.

At the time of enrollment, patients' demographic and clinical data were collected. Disease severity in patients of both groups was evaluated according the Clinical Pulmonary Infection Score (CPIS), which is a clinical score of 0–12 points based on six variables (Table 1), each variable was scored on a scale of 0-2 and CRIS score > 6 indicates presence of VAP (14, 15). Patients were also evaluated using the Acute Physiology and Chronic Health Evaluation II (APACHE II) score (16).

Laboratory investigations

A- Sterile endotracheal aspirate (ETA) was obtained from patients of both groups on day of enrolment in the study (D0). Samples was collected, processed and plated for culture. For definite diagnosis of VAP, 105 CFU/ml was considered as threshold and growth of any organism below the threshold was considered negative for VAP (17). Antibiotic sensitivity testing was performed and zone diameter was measured and interpreted according to guidelines of the Clinical and Laboratory Standards Institute (18).

B- Venous blood samples were collected, prior to initiation of antimicrobial therapy, by venipuncture under complete aseptic conditions on D0 and D4. Blood samples were collected in a plane container, allowed to clot then serum was separated by centrifugation at 3000 rpm for 10 min and serum was removed to be stored at -80°C until ELISA assayed for serum levels of PCT (RayBio, Parkway, Norcross, USA) (19) and CRP (Quantikine ELISA kit from R & D Systems, Inc., Minneapolis) (20).

Management

- Patients were managed according to the Surviving Sepsis Campaign guidelines (21). Empirical antimicrobial therapy was started on D0 once ETA samples were obtained and was modified according to the results of the cultures and sensitivity tests. Fluid resuscitation was conducted using crystalloid given at a minimum rate of 30 ml/kg (22) to achieve increased systolic arterial pressure (SAP) by ≥20 mmHg (23).

- Mechanical ventilation, physiotherapy and airway management were performed according to feasibility. Patients were categorized according to progress into Survivors who were discharged through or at the end of 28-days after enrolment and Non-survivors who had died through 28 days after enrolment.

Outcome measures

- Determination of 28-day survival rate for both groups

- The predictability of clinical scorings; APACHE II and CPIS scores, and D0, D4 levels of CRP and PCT and percentage of change of D4 levels in relation to D0 levels (= [(D4-D0)/ (D0)]/100) for mortality.

- Durations of MV, ICU stay and total hospital stay.

Statistical analysis

Sample size was calculated using the standard nomogram proposed by **Kraemer & Thiemann** [24] and a sample size of ≥40 patients was determined to be sufficient to detect a difference at the 5% significance level and give the trial 80% power [25]. Sample size and power were re-calculated and assured using Power and Sample Size Calculation Software program provided by Department of Biostatistics, Vanderbilt University. Results were analyzed using One-way ANOVA with post-hoc Tukey HSD Test and Chi-square test (X^2 test). Receiver operating characteristic (ROC) curve analysis judged by the area under the curve (AUC) compared versus the null hypothesis that AUC=0.05 and Regression analysis (Stepwise method) were used for stratification of studied parameters as specific predictors. Statistical analysis was conducted using IBM SPSS (Version 23, 2015) statistical package. P value <0.05 was considered statistically significant.

Results

Ninety patients developed manifestations suggestive of VAP; 53 patients fulfilled the VAP diagnostic criteria (VAP group); while 37 patients did not fulfill VAP diagnostic criteria (No VAP group). Sixteen VAP patients (30.2%) had early VAP, while 27 patients (69.8%) had late VAP. VAP patients showed significantly higher mean APACHE II and CPIS scores with significantly higher frequency of patients had APACHE II score of >20 and CPIS > 6 compared to No VAP group. Moreover, VAP patients had significantly lower SAP measures than No VAP patients. Details of clinical findings of studied patients are shown in table 1

Throughout 28-day, 32 patients died for a total 28-day MR of 35.6% with significantly higher MR among VAP patients, among patients had late VAP than patients had early VAP and among VAP females than males. Calculated APACHE II and CPIS scores were significantly higher in non-survivors compared to survivors in both groups and in VAP than in No VAP patients. Hemodynamic data showed non-significant between patients of both groups; apart from SAP measures that were significantly higher in survivors than non-survivors. Details of clinical data of studied patients categorized according to survival are shown in table 2.

Mean D0 serum CRP level was significantly higher in VAP patients than in No VAP patients and in non-survivors of both groups compared to survivors. All patients showed significantly lower D4 serum CRP levels compared to corresponding D0 levels with significantly lower levels in No VAP survivors than in VAP survivors. Percentage of change of serum CRP level was significantly higher in No VAP survivors compared to VAP survivors (Table 3).

Mean D0 serum PCT levels were significantly higher in VAP patients than in No VAP patients and in non-survivors compared to survivors in both groups. Survivors of both groups showed significantly lower D4 serum PCT levels compared to their D0 levels. In comparison to D0 serum PCT levels, D4 were significantly lower in VAP non-survivors but were non-significantly lower in No VAP non-survivors. Mean D4 serum

Table (1): Enrolment clinical data of studied patients

			VAP (n=53)	No VAP (n=37)	P value
Age (years)			57±12.1	54.5±12.9	=0.347
Male: Female			33: 20	21: 16	=0.766
Associated co-morbidities	No co-morbidities problem		50 (56.6%)	23 (62.2%)	=0.652
	Frequency/affected patient		1.24	1.16	=0.893
Type of undertaken surgical procedure or condition	CABG		13 (24.5%)	8 (21.6%)	=0.843
	Cancer surgery		7 (13.2%)	4 (10.8%)	
	Major surgeries		11 (20.8%)	8 (21.6%)	
	Multiple trauma		14 (26.4%)	11(29.8%)	
	Burn		8 (15.1%)	6 (16.2%)	
APACHE II score	Mean (±SD)		19±6.2	13.5±4.1	=0.001
	>20		18 (34%)	4 (10.8%)	=0.012
Septic status	Sepsis		39 (73.6%)	22 (59.5%)	=0.676
	No sepsis		14 (26.4%)	15 (40.5%)	
CPIS score	Temperature (°C)	Mean (±SD)	38.4±0.8	38±0.4	=0.010
		Score (0:1:2)	24:18:11	33:3:1	<0.001
	TLC (10^3 leukocytes/ ml)	Mean (±SD)	8.9±3.7	9±1.1	=0.829
		Score (0:1:2)	27:11:15	37:0:0	<0.001
	Tracheal secretions score (0:1:2)		14:25:14	11:23:3	=0.088
	Pa_{O2}: Fi_{O2} (mmHg)	>240 (score=0)	33 (62.3%)	29 (78.4%)	=0.104
		≤240 (score=2)	20 (37.7%)	8 (21.6%)	
	Chest X-ray score (0:1:2)		4:30:19	17:20:0	<0.001
	Culture of ETA	Score (0:1:2)	0:28:25	20:17: 0	<0.001
	Total CPIS score	Mean (±SD)	6±2.9	2.4±1.9	=0.001
		Score >6	21 (39.6%)	0	<0.001
Hemodynamic data	HR (beats/min)		89.8±9.1	84.2±15.4	=0.074
	SAP (mmHg)		98.8±13.3	103.6±9.9	=0.038
	DAP (mmHg)		66.4±7.7	67.6±11.7	=0.056
	MAP (mmHg)		77.2±8.9	78.6±13.4	=0.067

Data are presented as mean±SD, ratios & numbers; percentages are in parenthesis; VAP: Ventilator-associated pneumonia; : CABG: Coronary artery bypass graft; APACHE II: Acute Physiology and Chronic Health Evaluation II; CPIS: Clinical Pulmonary Infection Score; TLC: Total leucocytic count: ETA: Endotracheal aspirate; HR:Heart rate; SAP: Systolic arterial pressure; DAP: Diastolic arterial pressure; MAP: Mean arterial pressure; p<0.05: indicates significant difference; p>0.05: indicates non-significant difference; p values: indicates significance of difference between both groups

Table (2): Clinical findings of studied patients categorized according to survival as a primary outcome

		VAP (n=53)			No VAP (n=37)		
Parameter	Outcome	Survivors (n=30)	Non-survivors (n=23)	P=	Survivors (n=28)	Non-survivors (n=9)	P
Age		54±13.1	61±9.6	0.036	53±13.8	59.2±8.6	0.209
Gender	Male	19 (35.8%)	14 (37.8%)	0.029	17 (45.9%)	4 (10.8%)	0.596
	Female	11 (20.8%)	9 (24.3%)		11 (29.7%)	5 (13.5%)	
APACHE II score	Mean (±SD)	17.1±4.9	21.6±6.8	0.001	12±2.8	18.4±3.9	0.010
		P_1=0.001	P_2=0.029				
	>20	6 (20%)	11 (47.8%)	0.031	0	4 (44.4%)	0.001
CPIS score	Mean (±SD)	4.8±2.3	7.7±2.8	0.001	1.8±1.6	4±2.1	0.002
		P_1=0.001	P_2=0.001				
	>6	6 (20%)	15 (65.2%)	0.001	0	0	
Hemodynamic parameters	HR (beats/min)	89.1±5	90.9±12.6	0.826	86±10.6	87.1±5.5	0.859
		P_1=0.582	P_2=0.713				
	SAP (mmHg)	102.9±13	93.4±22.4	0.019	105.1±6.7	98.7±15.8	0.458
		P_1=0.867	P_2=0.635				
	DAP (mmHg)	67.8±6.9	64.6±8.4	0.341	70.5±5.2	65.8±7	0.289
		P_1=0.457	P_2=0.891				
	MAP (mmHg)	79.5±8.2	74.2±9	0.06	82±3.9	76.7±9.1	0.262
		P_1=0.568	P_2=0.804				

Data are presented as mean±SD & numbers; percentages are in parenthesis; VAP: Ventilator-associated pneumonia; APACHE II: Acute Physiology and Chronic Health Evaluation II; CPIS: Clinical Pulmonary Infection Score; HR: Heart rate; SAP: Systolic arterial pressure; DAP: Diastolic arterial pressure; MAP: Mean arterial pressure; p<0.05: indicates significant difference; p>0.05: indicates non-significant difference; P values indicates significance of difference between survivors and non-survivors in both groups; P_1 values indicates significance of difference between survivors in both groups; P_2 values indicates significance of difference between non-survivors in both groups

Table (3): Levels of serum CRP and PCT estimated at D0 and D4 with the percentage of change in studied patients categorized according to survival

Parameter		Group Outcome	VAP Total (n=53)	VAP Survivors (n=30)	VAP Non-survivors (n=23)		No VAP Total (n=37)	No VAP Survivors (n=28)	No VAP Non-survivors (n=9)
Serum CRP (mg/dl)	D0		139.3±30.5	129.5±33.6	152±20.3		118.9±33.9	111.5±30.4	142±35.7
		P=	0.004	0.108	0.808				
		P_1=			0.039	P_1=			0.045
	D4		98.5±22.1	95.8±25.2	102±17.2		75±24.4	67.4±20	98.7±22.1
		P=	0.001	0.001	0.916				
		P_1=			0.707	P_1=			0.001
		P_2=	0.001	0.001	0.001	P_2=	0.001	0.001	0.007
	%		28.6±9.7	25.8±7.3	32.3±11.3		37.3±8	39.8±6.9	29.7±6.2
		P=	0.001	0.001	0.826				
		P_1=			0.029	P_1=			0.001
Serum PCT (ng/ml)	D0		3.94±2.11	2.47±0.8	5.87±1.67		1.36±0.5	1.21±0.4	1.84±0.51
		P=	0.001	0.014	0.001				
		P_1=			0.001	P_1=			0.001
	D4		3±1.89	1.62±0.54	4.77±1.48		1.05±0.4	0.92±0.29	1.44±0.44
		P=	0.001	0.010	0.001				
		P_1=			0.001	P_1=			0.365
		P_2=	0.015	0.001	0.022	P_1=	0.004	0.003	0.099
	%		27.7±9.9	34±7.7	19.5±5.1		23.2±5.4	23.5±6	22.2±3.4
		P=	0.014	0.001	0.678				
		P_1=			0.001				0.896

Data are presented as mean±SD; VAP: Ventilator-associated pneumonia; CRP: C-reactive protein; PCT: procalcitonin; %: the percentage of difference between D4 and D0 levels; p<0.05: indicates significant difference; p>0.05: indicates non-significant difference; P values indicates significance of difference between both groups; P_1 values indicates significance of difference between survivors and non-survivors in both groups; P_2 values indicates significance of difference between D4 and D0 levels in both groups

Table (4): ROC analysis of clinical scores and laboratory findings as predictor for development and outcome of VAP

Variable		Prediction of VAP			Prediction of survival of VAP patients		
		AUC	P	95% CI	AUC	P	95% CI
APACHE II		0.765	<0.001	0.667-0.863	0.286	0.008	0.142-0.431
CPIS score		0.885	<0.001	0.819-0.951	0.178	<0.001	0.065-0.290
Serum CRP	D0	0.668	0.007	0.556-0.780	0.306	0.016	0.164-0.448
	D4	0.766	<0.001	0.665-0.867	0.483	0.836	0.324-0.428
	%	0.253	<0.001	0.150-0.357	0.278	0.006	0.127-0.428
Serum PCT	D0	0.934	<0.001	0.888-0.980	0.033	<0.001	0.008-0.073
	D4	0.904	<0.001	0.845-0.962	0.014	<0.001	0.009-0.036
	%	0.622	0.049	0.508-0.737	0.932	<0.001	0.868-0.996

VAP: Ventilator-associated pneumonia; AUC: Area under curve; APACHE II: Acute Physiology and Chronic Health Evaluation II; CPIS: Clinical Pulmonary Infection Score, CRP: C-reactive protein; PCT: procalcitonin; %: the percentage of difference between D4 and D0 levels; p<0.05: indicates significant difference; p>0.05: indicates non-significant difference

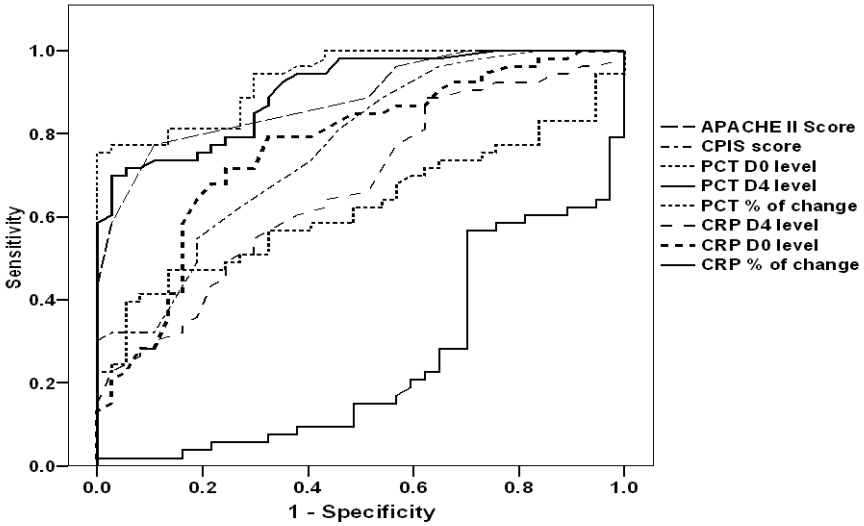

Fig. (1): ROC curve analysis of dinical and laboratory data as predictors for development of VAP

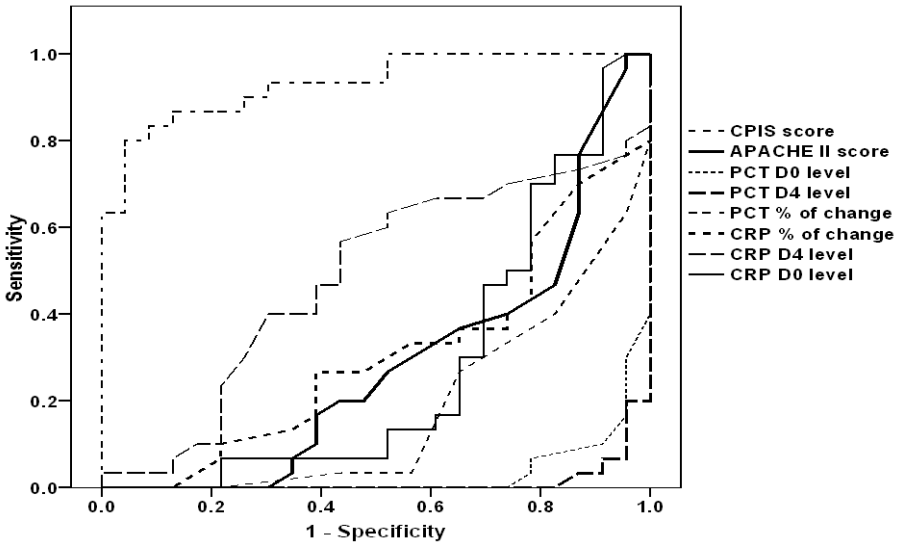

Fig. (2): ROC curve analysis of dinical and laboratory data as predictors for survival of VAP patients

Table (5): Regression analysis of clinical scores and laboratory findings as predictor for development of VAP

	Model No.	Variable	β	P
Prediction of VAP diagnosis	1	CPIS score	0.256	0.005
		D4-D0% of change of serum CRP	-0.237	0.001
		D0 serum PCT levels	0.511	<0.001
		D4-D0% of change of serum PCT	0.345	<0.001
	2	CPIS score	0.350	<0.001
		D4-D0% of change of serum CRP	-0.338	<0.001
		D0 serum PCT levels	0.337	0.001
	3	CPIS score	0.578	<0.001
		D4-D0% of change of serum CRP	-0.342	<0.001
	4	CPIS score	0.631	<0.001
Prediction of VAP patients' survival	1	D4 serum PCT levels	-0.540	<0.001
		CPIS score	-0.228	0.006
		D4-D0% of change of serum PCT	0.248	0.022
	2	D4 serum PCT levels	-0.721	<0.001
		CPIS score	-0.236	0.006
	3	D4 serum PCT levels	-0.833	<0.001

Table (6): Duration of MV, ICU and hospital stay of both groups categorized according to survival outcome

Group / Parameter		VAP			No VAP		
		Survivors (n=30)	Non-survivors (n=23)	Total (n=53)	Survivors (n=28)	Non-survivors (n=9)	Total (n=37)
Duration of MV (days)		7.3±2	9.4±2.6	8.2±2.5	5±1	6.4±0.7	5.4±1.1
	P1	0.001	0.001	0.001			
	P2	0.001			0.175		
Duration of ICU stay (days)		9.6±2.1	12±2.8	10.6±2.7	6.9±1.4	7.8±1.3	7.1±1.4
	P1	0.001	0.001	0.001			
	P2	0.001			0.119		
Duration of hospital stay (days)		13.3±3.8	17±5.3	14±4.3	9.1±2.8	16±2	9.8±3.4
	P1	0.039	0.001	0.001			
	P2	0.001			0.406		

Data are presented as mean ± SD; VAP: Ventilator-associated pneumonia; MV: mechanical ventilation; $p<0.05$: indicates significant difference; $p>0.05$: indicates non-significant difference; P_1 values indicates significance of difference between total patients, survivors and non-survivors in both groups; P_2 values indicates significance of difference between survivors and non-survivors of both groups

PCT levels were significantly lower in VAP survivors, but were non-significantly lower in No VAP survivors compared to corresponding non-survivors. Percentage of change of serum PCT levels were significantly higher in VAP survivors compared to No VAP survivors with non-significant difference between non-survivors of both groups and was significantly higher in VAP survivors than in non-survivors, while the difference was non-significant between No VAP patients (Table 3).

ROC curve analysis defined high D0 and D4 PCT levels, CPIS score, D4 CRP levels and APACHE II score as significant positive predictor for VAP diagnosis, in decreasing order of significance (Fig. 1). On the other hand, low D0 and D4 serum PCT levels, and low CPIS score are significant predictors for survival of VAP patients, while high percentage of change of serum PCT levels is the significant sensitive indicator of survival (Table 4, Fig. 2).

Regression analysis defined persistently high CPIS score as a significant positive predictor for VAP diagnosis and its significance increased progressively with exclusion of other predictors. Low percentage of decrease of serum CRP levels, high D0 serum PCT level and low percentage of decrease of serum PCT are also positive predictors for VAP diagnosis, in decreasing order of significance. Also, regression analysis defined persistent elevation of serum PCT till D4 as a significant negative predictor for survival of VAP patients and its significance increased progressively with exclusion of other predictors. Elevated CPIS scores and low percentage of decrease of PCT levels are also significant negative predictors for survival of VAP patients (Table 5).

Discussion

Majority of VAP patients had either multiple trauma patients (26.4%), CABG surgery (24.5%) or had burn (15.1%). Such frequencies point to the higher liability of these patients to develop VAP and go in hand with Tamayo et al.(27) who found VAP development after cardiopulmonary bypass is the most important independent risk factor for in-hospital mortality and Ranjan et al. (28) also

documented that trauma was a common underlying condition associated with VAP.

The 28-day MR of total studied patients was 35.6% with significantly higher MR among VAP patients than No VAP group (43.3% vs. 24.3%). These figures coincided with that previously reported in literature (29, 30, 31, 32). Moreover, Tamayo et al. (27) reported that patients with VAP had greater in-hospital mortality (49.2% vs. 2.0%) compared to patients without VAP and Sen et al. (33) found mortality was higher in burn patients who developed VAP (34% vs. 19%) than burn patients without VAP. The currently reported MR among VAP patients was significantly higher with late than early VAP (48.6% vs. 31.3%); similarly Vallés et al. (34) found VAP is associated with excess mortality, mostly restricted to late-onset VAP.

Interestingly, MR was significantly higher among VAP female patients than VAP male patients (37.8% vs. 24.3%) despite of the higher frequency of males developed VAP. This finding supported that previously reported by Sharpe et al. (35) who found females develop less VAP but experience increased mortality and increased characteristics of severe VAP in females may contribute to this observed mortality difference versus males

Patients of VAP group showed significantly longer duration of MV, ICU stay and hospital stay compared to No VAP patients. However, VAP survivors showed significantly shorter durations than non-survivors. Similarly, Tamayo et al. (27) reported that patients with VAP had a longer length of hospitalization than patients without VAP and Vallés et al. (34) and Nakaviroj et al. (36) found median duration of ventilator and ICU lengths of stay were longer in the VAP group.

Calculated APACHE II and CPIS scores were significantly higher in non-survivors compared to survivors in both VAP and No VAP groups with significantly higher scores in VAP than in No VAP patients. In line with these data, Karatas et al. (32) reported that high APACHE II is a significant risk factor for VAP and Zhou et al. (30) and Huang et al. (37) found APACHE II and CPIS scores were significantly higher in non-survivors compared to survivors and.

Regression analysis defined high CPIS score, high D0 PCT level and low percentages of decrease of CRP and PCT levels are positive predictors for VAP diagnosis, while persistent elevation of serum PCT till D4, elevated CPIS scores and low percentage of decrease of PCT levels are significant negative predictors for survival of VAP patients.

These findings go in hand with Sotillo-Díaz et al. (38) who reported that high serum PCT levels were associated to an increased risk of suffering VAP with sensitivity, specificity, and diagnostic odds ratio of 76%, 79% and 17.9, respectively and its diagnostic yield was not modified by the type of critically ill patient or the time to VAP occurrence, but by prior exposure to antibiotics. Li et al. (39) also reported that multivariable Cox regression model showed that high serum PCT level was independently associated increased risk of morality within 2 months after VAP diagnosis. Moreover, Tanrıverdi et al. (40) found serum PCT to be a superior prognostic marker compared to CRP for predicting mortality in critically ill VAP patients and PCT level on D3 was the strongest predictor of mortality in VAP.

Recently, Liu et al. (41) documented that for critically ill VAP patients, an elevated PCT level was associated with an increased risk of mortality. On the other hand, Póvoa et al. (42) found the slope of CRP change over time, the highest CRP ratio concentration and Δ (max) CRP during the first 6 days of MV were all significantly associated with VAP development. However, Muzlovic et al. (43) found both CRP and PCT showed comparable results for VAP diagnosis with AUC of 0.869 and 0.909, respectively.

The obtained results indicate the possibility of reliance on estimation of serum PCT coupled with CPIS score as diagnostic and prognostic parameters for VAP patients. In line with this assumption, Su et al. (44) reported that for 28-day survival, PCT level combined with CPIS score was the most reliable for prognostic assessment for VAP patients. Also, Zagli et al. (45) found the newly proposed Chest Echography and Procalcitonin Pulmonary Infection Score (CEPPIS) that was based on chest echography, PCT level and CPIS score was significantly better in predicting VAP than CPIS with higher sensitivity and specificity and an AUC indicating significantly higher diagnostic value for CEPPIS. Recently, in 2017, İşgüder et al. (46) found VAP suspicion patients had significantly higher PCT levels compared to control group and VAP confirmed cases had higher PCT and CPIS levels compared to non-confirmed VAP cases and so concluded that PCT and CPIS variables are independent risk factors for VAP.

Conclusion

VAP had deleterious on patients maintained on MV with high 28-day mortality rate. No single clinical or laboratory parameter could assure VAP diagnosis or predict prognosis. Reliance on combined evaluation of CPIS score and estimation of serum PCT levels improved the ability to diagnose VAP and low levels of both parameters are independent predictors of survival. Sequential estimation of PCT allows evaluation of response to applied therapeutic lines and so improves the survival predictability.

Conflict of Interest

No Conflict of Interest

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