RESEARCH ARTICLE

A Comparison of Acute Physiology and Chronic Health Evaluation II Score and Serum Procalcitonin Change for Predicting Mortality in Acute Pancreatitis

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Abstract

Introduction: The prediction of mortality in acute pancreatitis (AP) is a useful estimate for effective treatment. Scoring systems such as acute physiology and chronic health evaluation (APACHE) II, computed tomography (CT) severity index (CTSI), bedside index of severity in acute pancreatitis (BISAP), etc., are used for prediction. Biomarkers like C-reactive protein (CRP) and procalcitonin (PCT) are also considered useful for prognostication. The aim of this retrospective study was to correlate the changes in serum PCT level with APACHE II score between admission and 48 hours as mortality predictor in AP.

Materials and methods: The observational study was conducted in a cohort of 42 patients admitted consecutively in the seven-bedded general intensive care unit (ICU) of our institute between June 2016 and May 2018, with the diagnosis of AP. The APACHE II score and serum PCT level at admission and 48 hours were retrieved from the hospital database. The change in APACHE II and PCT level was compared between ICU "survivors" and "nonsurvivors." The predictive accuracy of APACHE II and PCT was measured using area under receiver–operator characteristics (ROC) curve. A p value <0.05 was considered as significant.

Results: Of the 42 patients enrolled, 30 patients (71.42%) were survivors and 12 (28.58%) were nonsurvivors. The median APACHE II score in nonsurvivors increased from 16 (7–19) to 23 (11–29) and remained unchanged at 16 (9–19 at admission; 10–22 at 48 hours) in survivors. The median PCT levels increased from 3.8 (1.2–5.6) to 6.2 (1.9–12.5) in nonsurvivors and decreased from 3.8 (1.2–5.6) to 2.2 (0.6–2.9) in survivors. Serum PCT change compared better than the APACHE II score change among survivors ($r = 0.455$, $p = 0.011$) with a mean (±standard deviation SD) change of 1.41 (±1.59).

Conclusion: The change in serum PCT and APACHE II between admission and 48 hours correlates well and is useful for mortality prediction in AP. Serum PCT change compares better than APACHE II score change in survivors.

Keywords: Acute pancreatitis, Acute physiology and chronic health evaluation II, Procalcitonin.

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Introduction

The incidence of organ failure and death in acute pancreatitis (AP) varies from 28% to 76% and 28% to 69%, respectively.[1–3] Therefore, the prediction of mortality is a pivotal consideration for choosing the right treatment strategy in such patients.

The different scoring systems such as bedside index of severity in acute pancreatitis (BISAP), acute physiology and chronic health evaluation (APACHE) II, Ranson's, etc., are conventionally used to grade severity and predict mortality in acute severe pancreatitis. The revised Atlanta classification of 2012 provides clear definitions to classify AP and makes assignment of scores easier using easily identifiable criteria.[4] However, so far no single scoring system has proven superior over another.

Serum procalcitonin (PCT) is a well-known marker for sepsis, systemic bacterial infection, and organ failure which is commonly used to guide antibiotic de-escalation in sick patients. Although many studies have highlighted its importance in predicting the severity of AP, there is lack of distinct comparison of its changes and its correlation with the prevailing severity scores in predicting mortality after AP.[5]

The aim of this retrospective observational study was to compare the changes in serum PCT level with APACHE II score between admission and 48 hours as mortality predictor in critically ill patients with AP.

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Materials and Methods

The observational study was conducted in a cohort of 42 patients admitted consecutively in the seven-bedded general intensive care unit (ICU) of our institute between June 2016 and May 2018 after seeking waiver for informed consent from the institutional ethics committee. The data were retrospectively extracted from hospital

database maintained for clinical and administrative purpose. All patients with the diagnosis of AP were eligible for enrollment. Only adult patients over 18 years of age with ICU length of stay for more than 2 days and available APACHE II scores and serum PCT levels at least during admission and 48 hours thereafter were included in the study.

The patients were categorized as survivors and nonsurvivors depending on their survival or death in the ICU. All demographic variables like age, sex, and comorbid conditions were retrieved and compared. The categorization into necrotizing and acute interstitial edematous pancreatitis based upon the revised Atlanta classification of 2012 was followed.[4] The presence or absence of necrosis on contrast-enhanced computed tomography performed within 48 hours of ICU admission was also noted for the confirmation of diagnosis.

The APACHE II scores and serum PCT levels measured at the time of ICU admission and 48 hours thereafter were retrieved and compared. The length of ICU stay and duration of mechanical ventilation were also retrieved.

For serum PCT, blood samples were centrifuged for 10 minutes at 3,000 rotations per minute at −4°C. The serum was removed and stored at −80°C until biochemical analysis. The serum PCT concentration was measured using a chemiluminescent immunoassay (LUMItest PCT; Brahms Diagnostica, Berlin, Germany). The reference value range established for this method was <0.05 ng/mL. The assay combined a one-step immunoassay sandwich method (Biomeriux, SA) with a final fluorescent detection in the wells containing anti-PCT antibodies labeled with alkaline phosphatize (conjugate). The concentrations were expressed in nanograms per milliliter and values >0.05 ng/mL were considered positive.

All statistical analyses were performed using software SPSS 24.0 (SPSS, Inc., Chicago, IL, USA). The results were expressed as medians followed by range or number followed by percentage. Student's *t* test for unequal variance was used to compare continuous variables like age, APACHE II scores, PCT levels, length of ICU stay, and duration of mechanical ventilation. Chi-square test was used to compare the categorical parameters such as sex, diagnostic classification, and etiology of AP among the two groups. The predictive accuracy of APACHE II scores and serum PCT levels at admission and 48 hours after admission was compared using the area under the receiver–operator characteristics (ROC) curve. The *p* value <0.05 was considered to indicate statistical significance.

Results

Of the 42 patients enrolled in our study, 30 patients (71.42%) were survivors and 12 (28.58%) were nonsurvivors.

No differences were observed between survivors and nonsurvivors with regard to their age, sex, etiology, comorbid conditions, length of stay in ICU, and the duration of mechanical ventilation in the ICU. The incidence of necrotizing pancreatitis (NP) and interstitial edematous (IE) pancreatitis was similar in the two groups ($p = 0.06$; $p = 0.07$) (Table 1).

The APACHE II scores between ICU admissions to 48 hours increased more significantly in the nonsurvivors compared to the survivors ($p < 0.001$, CI = 5.35–12.68) (Table 2).

The increase in serum PCT levels during the same time frame was also significant among the nonsurvivors ($p < 0.001$, CI = 1.92–4.30). But the Serum PCT change compared better than the APACHE II score change among survivors ($r = 0.455$, $p = 0.011$) with a mean reduction of 1.41 U PCT from the time of admission to 48 hours with a standard deviation of 1.59 (paired $t = 4.861$, df—29 and $p < 0.001$) (Table 3 and Fig. 1).

The ROC curve of APACHE II score (area under curve, AUC = 0.453) and PCT (AUC = 0.315) levels (Fig. 2 and Table 4) at admission demonstrated positive correlation in both survivors and nonsurvivors in predicting mortality.

Table 1: Table showing demographic and clinical profile of survivors and nonsurvivors

		Survivors (n = 30)	*Nonsurvivors (n = 12)*	*p value*
Age (years)*		49 (67–27)	49 (67–37)	0.52
Sex (M/F)**	Male	23 (74.2%)	8 (25.8%)	0.5
	Female	7 (63.6%)	4 (36.4%)	
Diagnosis**	NP	24 (80%)	6 (30%)	0.07
	IE	6 (50%)	6 (50%)	0.06
Etiology**	Gallstones	21 (72.4%)	8 (27.6%)	0.83
	Alcoholism	15 (68.2%)	7 (31.8%)	0.62
Length of stay (days)*		10.5 (16–4)	7 (14–3)	0.28
Duration of mechanical ventilation (days)*		6.5 (13–2)	7 (14–3)	0.74
Infection**		6 (20%)	4 (33%)	0.64
No. of patients on prophylactic antibiotics**		5 (16%)	2 (16%)	0.9

*Median (range), ** number (percentage)
NP, necrotizing pancreatitis; IE, interstitial edematous pancreatitis
#$p < 0.05$

Table 2: Table showing change in acute physiology and chronic health evaluation II score from admission to 48 hours

	APACHE II (admission)	*APACHE II (48 hours)*	*p value*
Survivors ($n = 30$)*	16 (9–19)	16 (10–22)	0.08
Nonsurvivors ($n = 12$)*	16 (7–19)	23 (11–29)	0.002#

*Median (range)
APACHE, acute physiology and chronic health evaluation
#$p < 0.05$

Table 3: Table showing change in procalcitonin level from admission to 48 hours

	PCT levels (admission)	*PCT levels (48 hours)*	*p value*
Survivors ($n = 30$)*	3.2 (1.4–3.8)	2.2 (0.6–2.9)	0.02#
Nonsurvivors ($n = 12$)*	3.8 (1.2–5.6)	6.2(1.9–9.1)	0.01#

*Median (range)
PCT, procalcitonin
#$p < 0.05$

Discussion

Our study found a positive correlation between the change of serum PCT and APACHE II from admission to 48 hours as mortality predictor in acute severe pancreatitis. It has also been found that

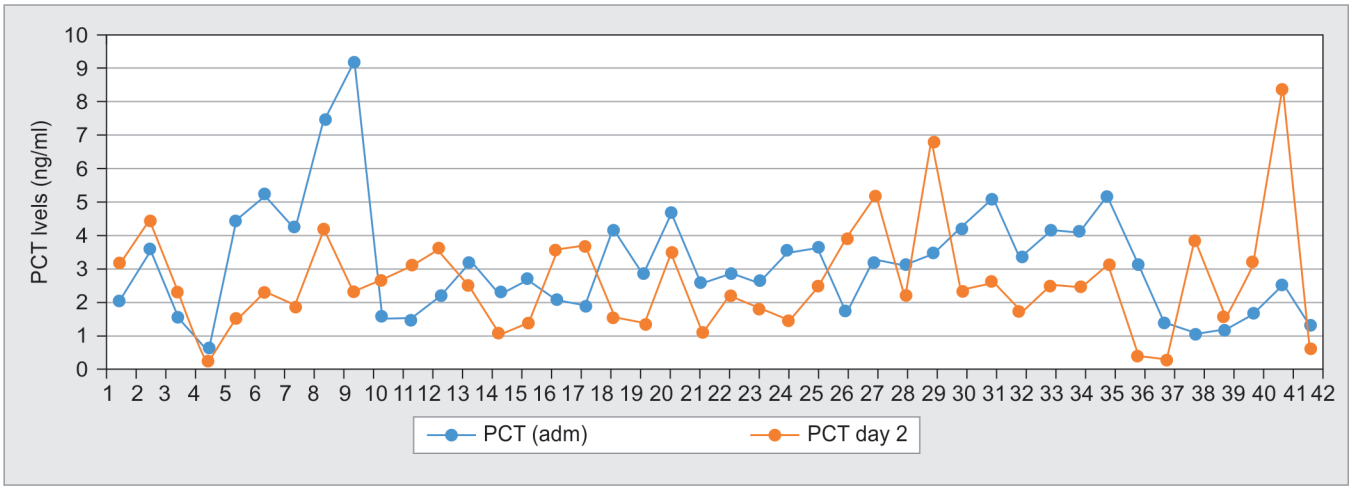

Fig. 1: Figure comparing changes in procalcitonin level in patients from admission to 48 hours

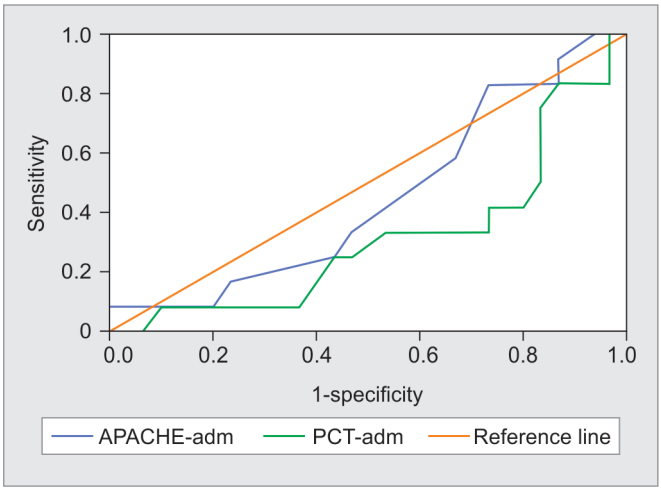

Fig. 2: Figure showing the area under receiver–operator characteristics curve changes for procalcitonin and acute physiology and chronic health evaluation II at 48 hours. ROC, receiver operating characteristic

Table 4: Table showing the AUC for acute physiology and chronic health evaluation II score and procalcitonin level for predicting mortality

	APACHE II score	*PCT levels*
AUC	0.453	0.315
Confidence interval	0.265–0.640	0.134–0.496
p value	0.064	0.636

[#]$p < 0.05$
AUC, area under curve; APACHE, acute physiology and chronic health evaluation; PCT, procalcitonin

the serum PCT change is a better predictor than APACHE II in survivors of AP.

The APACHE II score has been used for discriminating complicated and uncomplicated pancreatitis from fatal pancreatitis since 1990 when a prospective study of 190 patients found no deaths, with peak APACHE II score of less than 10 within the first 3 days of hospital admission.[6] Since then many studies have compared and confirmed the usefulness of APACHE II in various settings of AP.[7,8] With the advancement of imaging techniques, more precise comparisons involving scores such as CT severity index (CTSI), BISAP score, Japanese severity score, harmless AP score, pancreatitis outcome prediction, sequential organ failure assessment, etc., ensued.[9,10] It was evident from their findings that these scores were no superior to APACHE II as mortality predictor in AP. Our study establishes that change in APACHE II score from admission to 48 hours is a useful mortality predictor of AP.

Procalcitonin, the precursor of hormone calcitonin, has been used in various clinical settings with specific cutoffs and clinical algorithms to aid the diagnosis of bacterial infection and sepsis. The more notable and corroborative evidences justified its use in the initiation and discontinuation of antibiotics during antibiotic stewardship programs.[11,12] Majority of the randomized controlled trials also demonstrated the safety and efficacy of PCT-guided antibiotic therapy. But apart from bacterial infections, certain other conditions like trauma, burns, prolonged cardiogenic shock, pancreatitis, malaria, fungal infections, etc., were also found to be associated with elevation of serum PCT. The cause for this is an increased PCT production in various parenchymal tissues mediated by cytokines like interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and interleukin-1β (IL-1β) surpassing their ability to cleave PCT to calcitonin causing accumulation.[13,14] Our study has duly confirmed this.

The patterns of cytokine evolution and rise in PCT in sepsis and septic shock have been investigated at great depths. Both PCT and IL-6 act as reliable acute phase reactants in experimental model of acute edematous pancreatitis, sterile pancreatic necrosis, and infected pancreatic necrosis in experimental rats.[15,16] The release of cytokines in AP is closely linked to the development of distant organ dysfunction. Both increased pancreatic expression of IL-1β and the inactivation of the IL-1 converting enzyme (ICE) have been found to result in milder pancreatitis and improved survival in experimental pancreatitis, whereas more systemic complications were found to be associated with increase in monocytic secretion of TNF-α, IL-6, and IL-8 in patients with complicated AP.[17,18] The pattern of PCT change observed in our study also confirms this view.

There was close correlation of serum PCT change and mortality in our study in both acute IE and NP. It has been shown in earlier studies that the concentration of IL-8 is increased in NP, whereas raised IL-6 is more equivocal for edematous pancreatitis. Since PCT has strong correlation with both the variables, any prognostication

based on PCT change may be more useful than either IL-6 or IL-8 alone.[19,20]

Our study has found better correlation between serum PCT changes from admission to 48 hours compared to APACHE II score in survivors of AP. There may be many reasons for the same. First, APACHE II has been accepted and validated with widely varying AUC from 0.46 to 0.74. The monitoring modality, the effectiveness of multidisciplinary team, the therapeutic preference, and the patient characteristics can all unduly affect the scoring pattern. Second, the APACHE II score is underestimated in assigning chronic health points in the presence of specific conditions such as stable angina II/IV New York Heart Association, mild emphysema, and diabetes mellitus that are not listed in the original description. Third, the importance of what constitutes as initial 24 hours gets muddled when the patient is stabilized and shifted from the emergency room or ward. Since the effect of stabilization is different in survivors and nonsurvivors, the APACHE II at ICU admission can disregard some abnormal values of hematocrit, creatinine, and sodium that may be missed initially. Lastly, there is sufficient scope for errors while calculating oxygenation using oxygenation formulas (alveolar–arterial oxygen gradient), disregarding low red cell count due to nontransfusion of red cells and attributing lower consciousness scores in Glasgow Coma Scale for drug-induced sedation.[21–23] All these justifications are applicable and valid in our study.

Our study has demonstrated consistent and uniform reduction in PCT in survivors of acute severe pancreatitis. There is a growing evidence to support that all the distant organ complications in AP are linked to lymphocyte activation and recovery to lymphocyte depletion.[24,25] Since both increased PCT production and lymphocyte activation follow the same pathway, a lack of "release" during recovery can reset the macrophage lymphocyte imbalance and produce consistent reduction in serum PCT. This change is much slower with prognostic variable like C-reactive protein (CRP).[26] Our study has vividly demonstrated this change and its relation to the falling APACHE II score in survivors during the recovery phase.

However, our study has several limitations. One, the exact timing of organ failure is not available in our study and only persistent organ failure is taken into consideration. Two, the persistence of a lag period between recording of APACHE II score and the performance of serum PCT can variably affect the observations. Third, the patients with recurrent pancreatitis undergoing drainage procedures prior to admission are unlikely to exhibit similar changes. Finally, all the drawbacks inherent in a retrospective design can impact our findings directly or indirectly.

To conclude, there has been no prognostic comparison between change in serum PCT and APACHE II score in AP so far. Our study shows decline and nondecline of both APACHE II scores and serum PCT after 48 hours of ICU admission in nonsurvivors and survivors, respectively. In survivors, serum PCT change compares better than APACHE II score change. However, larger prospective studies can elucidate more facts pertaining to specific advantages and disadvantages.

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