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A Comparison of the Ranson Score and Serum Procalcitonin for Predicting the Severity of Acute Pancreatitis

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Abstract: ***Introduction: Early identification of patients who develop severe acute pancreatitis would enable the selection of patients from early intensive management. Because severe acute pancreatitis is characterized by the development of systemic inflammation, a prospective study was conducted to study whether procalcitonin, a marker of systemic inflammation, differentiated between patients with mild and severe pancreatitis. Purpose: The present prospective study was carried out to evaluate the relevance of procalcitonin as a predictor of disease severity. Methods: A prospective study was conducted on 40 patients presenting with acute pancreatitis in department of general surgery, JSS Hospital Mysuru from October 2014 to October 2016. Procalcitonin levels was measured by Electrochemiluminescence immunoassay. The accuracy of procalcitonin in predicting severe acute pancreatitis was compared with Ranson's score. Results: Of the 40 patients 24 patients had severe pancreatitis and 16 had mild pancreatitis. Sensitivity, specificity, Positive predictive value and Negative predictive value for patients calculated using procalcitonin level at 0.5 ng/ml, Ranson's score at 3 were 25%,94%,86%,46% and 46%,81%,79%,50% respectively. Conclusion: The available data indicates that in acute pancreatitis RANSON score correlated better than serum procalcitonin in predicting the progression to severe pancreatitis .***

Keywords: Pancreatitis, Procalcitonin, Ranson's score

1. Introduction

Acute pancreatitis is an acute inflammatory process ranging clinically from mild discomfort with localized inflammation to severe disease involving remote organ systems. There is a continuum from the development of systemic inflammatory response syndrome (SIRS)[1] to the onset of multiple organ dysfunction (MODS), which is seen in about 24 per cent of patients with acute pancreatitis and carries the highest mortality rate of 36 per cent[2,3].Diagnosis is based on the presence of at least two of the following three features: abdominal pain; increased pancreatic amylase, and/or lipase levels to ≥3 times the upper limit of normal; and imaging tests showing characteristic findings of acute pancreatitis.[4]

Several inflammatory markers are being used routinely in various hospitals in India to assess the prognosis of patients with acute pancreatitis. Among these are the total and differential leukocyte counts, erythrocyte sedimentation rate, and CRP. Various scoring systems such as the RANSON scores have also been used to stratify patients with acute pancreatitis.

Procalcitonin is a calcitonin propeptide (molecular mass 13 kDa) made up of 116 amino acids. It is reported to increase early in severe infection and inflammation.[5,6.]

Several studies on plasma PCT have demonstrated its role in the diagnosis of sepsis, prognosis of acute severe pancreatitis, and even as a prognostic marker following major surgery.[7-11] Beyond its value for the diagnosis of sepsis, PCT has also proved to be useful in monitoring the course and severity of the systemic inflammatory response. There are noninfectious conditions causing elevation in PCT levels. These include the following:

1) **The first day(s) after**
a) A major trauma
b) Major surgical intervention
c) Severe burns
d) Treatment with OKT3 antibodies and other drugs stimulating the release of proinflammatory cytokines
e) Birth in neonates (age less than 48 h)

2) **Patients with**
a) Prolonged or severe cardiogenic shock
b) Prolonged severe organ perfusion abnormalities
c) Small cell lung cancer or medullary C cell carcinoma of the thyroid

In this study we investigated the validity of procalcitonin as a biochemical marker in the early diagnosis of acute pancreatitis and for monitoring prognosis in mild and severe cases.

2. Materials and Methods

Source of Data
The sources of data were all patients presenting with acute pancreatitis to the department of general surgery JSS Hospital, Mysuru from October 2014 to October 2016.

Sample Size
A total of 40 patients were included in the study. Institutional Ethical Review Board clearance was obtained for the study.

Exclusion Criteria
1. History of trauma
2. Prolonged cardiogenic shock with impaired organ perfusion

3. Lung cancer or medullary carcinoma of the thyroid

Study Design
Observational study—prospective study design

Protocol of the Procedure
1) Inclusion and exclusion criteria were applied to all patients presenting with acute pancreatitis.
2) Patients were educated about the study and only those patients consenting to participate in the study were included.
3) Database collection included documentation of medical history, age, sex, prehospital interval, vital signs, abdominal signs, and drug history.
4) Serum procalcitonin level determination was performed on the same serum sample drawn for other biochemical tests.
5) Plasma procalcitonin was estimated using Electrochemiluminescence immunoassay.
6) Descriptive and inferential statistical analysis was carried out on the data collected using SPSS 21.0

3. Results

Out of the total of 40 patients 34 patients (85%) were males and 6 were females with a mean age of 42.6years (range, 16-70 years). Eighteen patients (37.5%) had recurrent pancreatitis and 25 patients (62.5%) gave history of consumption of alcohol within 72 hr of presentation. In 28 patients (70%), ethanol abuse was found to be the cause for pancreatitis while 4 patients (10%) had gall stone pancreatitis. In 4 patients (10%) no etiological factor was found and these patients were diagnosed to have acute idiopathic pancreatitis.

Serum procalcitonin was found to be raised in all patients (normal value 0.005ng/ml), out of them 7 patients had value >0.5ng/ml. 14 patients (35%) had total RANSON score ≥ *3*.

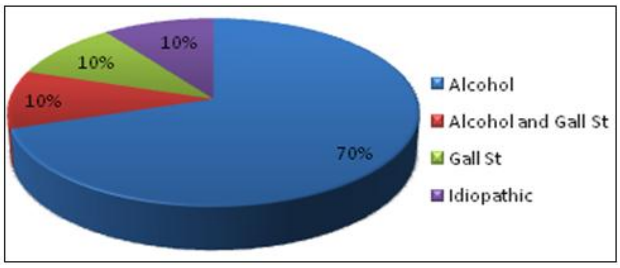

Figure 1: Pie diagram showing etioloical factors for acute pancreatitis

RANSON score and procalcitonin levels versus Hospital stay
As can be seen from table 1, there was only positive correlation between PCT levels and RANSON score. There was no significant correlation between PCT levels and RANSON score with total hospital stay as well as ITU and ICU stay.

Table 1: Correlation coefficients for hospitalization

			PCT	RANSON Score	Hospital Stay days	ITU Stay	ICU Stay
Spearman's rho	Serum Procalcitonin	Correlation Coefficient	1	.372*	0.06	0.213	0.113
		p		0.02	0.714	0.192	0.486
		N	40	39	40	39	40
	RANSON Score	Correlation Coefficient	.372*	1	-0.046	0.268	0.004
		p	0.02		0.782	0.104	0.979
		N	39	39	39	38	39

P >0.05 is significant

RANSON Score and procalcitonin levels in predicting Severe acute pancreatitis.

Out of total 40 patients 24 patients had severe pancreatitis. 16 patients developed ARDS 1 patient had AKI, 1 patient developed MODS. 13 patients developed local complications. By CT only 3 patient had pancreatic necrosis. There was no mortality.

Figure 2 and table 2 shows the receiver operating characteristic (ROC) curves for severe acute pancreatitis. Using ROC curves, a cut off value of >0.5ng/ml at admission for serum procalcitonin was only 25% sensitive but 94% specific for predicting severe acute pancreatitis.

In all the patients with acute pancreatitis the serum PCT was above the normal limit(0.05ng/ml). Sensitivity and specificity values for patients with severe pancreatitis calculated with PCT level >0.5ng/ml, RANSON score at 3 were 25%, 94%, 46% and 81% respectively.(Table 3,4,5,6).

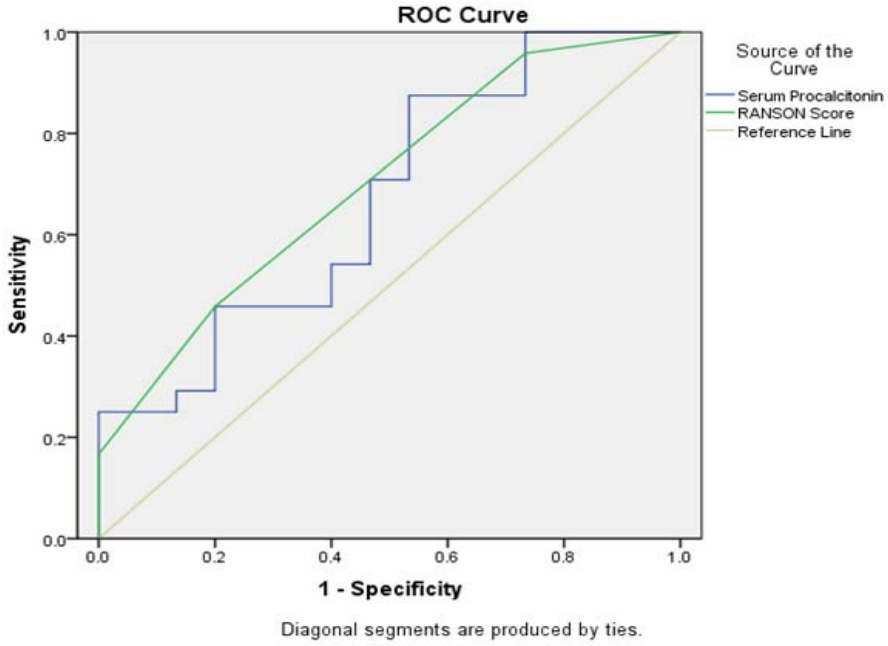

Figure 2: Receiver operating characteristic (ROC) curves for severe pancreatitis

Table 2: Area under curve (AUC) for variables predicting severe pancreatitis.

Test Result Variable(s)	Area	p	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
Serum Procalcitonin	0.669	0.078	0.492	0.847
RANSON Score	0.701	0.036	0.535	0.868

Table 3: RANSON score in patients with acute pancreatitis

		Severe Pancreatitis	
		Yes	No
		Count	Count
Ransons score category	≥3	11	3
	<3	13	13

Table 4: Sensitivity, specificity, predictive values, diagnostic accuracy and likelihood ratios of RANSON score ≥3 for discrimination of severe pancreatitis

Parameter	*Estimate*	*Lower - Upper 95% CIs*
Sensitivity	45.83%	(27.89, 64.93)
Specificity	81.25%	(56.99, 93.41)
Positive Predictive Value	78.57%	(52.41, 92.43)
Negative Predictive Value	50%	(32.06, 67.94)
Diagnostic Accuracy	60%	(44.6, 73.65)
Likelihood ratio of a Positive Test	2.444	(1.03 - 5.799)
Likelihood ratio of a Negative Test	0.6667	(0.5538 - 0.8026)

Table 5: Serum Procalcitonin levels in patients with acute pancreatitis

		Severe Pancreatitis	
		Yes	*No*
		Count	*Count*
Serum Procalcitonin category	>0.5	6	1
	<0.5	18	15

Table 6: Sensitivity, specificity, predictive values, diagnostic accuracy and likelihood ratios of PCT level >0.5ng/ml for discrimination of severe pancreatitis

Parameter	*Estimate*	*Lower - Upper 95% CIs*
Sensitivity	25	(12, 44.9)
Specificity	93.75	(71.67, 98.89)
Positive Predictive Value	85.71	(48.69, 97.43)
Negative Predictive Value	45.45	(29.84, 62.01)
Diagnostic Accuracy	52.5	(37.5, 67.06)
Likelihood ratio of a Positive Test	4	(0.2115 - 75.66)
Likelihood ratio of a Negative Test	0.8	(0.7112 - 0.8998)

4. Discussion

The most important step in the diagnosis and treatment of acute pancreatitis is differentiation between severe and mild cases. Contrasted dynamic computerized tomography that shows pancreatic and peri-pancreatic necrosis is the gold standard in differentiating between acute edematous or necrotizing pancreatitis. Another advantage of computerized tomography is the possibility of taking percutaneous samples for bacterial investigation in the presence of necrosis.[12,13]

Scoring systems are employed in order to determine the severity of acute pancreatitis as soon as possible and to identify any need for intensive care. To determine the Ranson score, which is used to establish the severity of pancreatitis, 11 parameters are evaluated and the waiting time is 48 h. The APACHE II scoring system, on the other hand, is a practical method that includes the patient's age and chronic disease state as well as 12 physiological values.[14] Thus there is a recognized need for a method for determining the severity of acute pancreatitis which can be applied daily, can easily be evaluated, which is practical and has a high rate of specificity and accuracy.

Procalcitonin is a glycoprotein that increases selectively in cases of bacterial inflammation, sepsis and multi-organ failure. In normal healthy individuals, procalcitonin is synthesized as the intra-cellular prohormone of calcitonin in the C cells of the thyroid gland and it is found at picogram levels in the plasma (~0.05 ng/ml). In cases of severe inflammations and sepsis, however, the plasma concentration ranges between 1 ng/ml and 1000 ng/ml; possible sources of this procalcitonin are neuroendocrine cells in the lungs and kidneys.[15,16] Procalcitonin levels can be measured by immunoluminometric and radioimmunoassay methods or semi-quantitatively by strip tests. In this study the measurement was made by a radioimmunoassay method.[17,18,19]

A large number of studies have assessed the role of plasma PCT and compared it to other inflammatory markers in predicting the severity of pancreatitis and the development of infected necrosis.[20-27] These studies have shown that plasma procalcitonin is a good marker for predicting severity and development of organ failure in acute pancreatitis and as well as predicting the development of infected pancreatic necrosis.

A prospective international multicenter study by Bettina M et al.[28] assessed the role of plasma PCT in the development of pancreatic infections and overall prognosis of severe acute pancreatitis. In their study, they monitored both plasma PCT and CRP values routinely and concluded that monitoring of plasma procalcitonin allows early and reliable assessment of clinically relevant infections and overall prognosis in acute pancreatitis and thereby contributed to improved stratification of patients at risk to develop major complications.

In our study, we analysed the role of serum procalcitonin levels using Electrochemiluminescence immunoassay in predicting the prognosis and predicting the progression te severe acute pancreatitis. There was no significant correlation between PCT levels with total hospital stay as well as ITU and ICU stay. Total RANSON score after 48 hours of admission correlated better than serum procalcitonin levels in predicting the progression to severe acute pancreatitis and organ failure.

Most of the studies conducted to predict the role of procalcitonin levels at admission in predicting acute severe pancreatitis used a semi quantitative strip test to assess the level of procalcitonin levels. In our study we used a radioimmunoassay which is more superior and accurate in predicting the procalcitonin levels.

A meta analysis conducted by Nusrat Shafiq et al.29 based on all relevant articles until November 2004 searched from MEDLINE and EMBASE regarding estimating the diagnostic accuracy of procalcitonin as a marker of the severity of acute pancreatitis which showed that procalcitonin cannot be considered a good marker for assessing the severity of pancreatitis.

In a prospective study by Byung Geun Kim et al.30 assessed the role of procalcitonin in early prediction severe acute pancreatitis and concluded that procalcitonin levels of 0.5ng/ml has only sensitivity and specificity of 87% and 24% respectively whereas RANSON score of ≥3 has sensitivity and specificity of 92% and 97% respectively.

5. Conclusion

In patients with acute pancreatitis, serum procalcitonin level at admission does not accurately predict the progression to severe acute pancreatitis. RANSON score correlated better than serum procalcitonin in predicting the progression to severe pancreatitis.

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