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Comparative Analysis of Serum Procalcitonin Levels with CT Severity Index in Acute Pancreatitis

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Abstract: ***Plasma procalcitonin (PCT) is a highly specific biomarker for the diagnosis of bacterial infection and sepsis. There are studies that have demonstrated its role in the setting of sepsis and acute pancreatitis. This study aims to analyze and compare the prognostic efficacy of serum procalcitonin level with CT severity Index in acute pancreatitis. A prospective observational study was conducted in the department of general surgery of Kempegowda Institute of medical Sciences and Research Centre from March 2021 to August 2022. Plasma procalcitonin was estimated and CT severity scoring was calculated. The study included a total of 51 patients diagnosed to have acute pancreatitis. Data was collected and statistically analyzed using SPSS version 22. All patients were males with a mean age of 42.29 years (range, 18-62 years) and all had ethanol-induced pancreatitis. Plasma PCT values were found to correlate better than CT severity index with the total duration of hospitalization, and ICU stay, as well as with the progression to severe acute pancreatitis. A cut off for plasma PCT of >0.5 ng/mL was found to be 100 % sensitive and 100 % specific for predicting the progression to severe acute pancreatitis. Plasma PCT also correlated well with number of days of hospitalization when compared to CT severity Index. Plasma procalcitonin serves as an early and dependable marker for predicting outcomes in acute pancreatitis.***

Keywords: Procalcitonin, Acute abdomen, Acute pancreatitis, CRP, PCT, CT severity index

1. Introduction

Procalcitonin (PCT) was first identified in 1984,[1] and since then, its biological properties and clinical significance have garnered significant attention. The elevated serum levels of PCT in septic patients were initially reported in 1993. Plasma procalcitonin (PCT) is a highly specific biomarker commonly used to assess systemic inflammation and infection, particularly in conditions such as sepsis, bacterial infections, and severe inflammatory diseases. Procalcitonin (PCT) is the peptide precursor to the hormone calcitonin, which plays a role in regulating calcium balance. PCT is formed when pre-procalcitonin is cleaved by endopeptidase. It consists of 116 amino acids and is primarily produced by the parafollicular cells (C cells) of the thyroid, as well as the neuroendocrine cells in the lungs and intestines. Under normal conditions, PCT is produced in the thyroid gland. However, during systemic bacterial infections or severe inflammatory responses, it is also synthesized by other tissues, such as the liver and lungs, in response to pro-inflammatory cytokines. In healthy individuals, PCT levels in the bloodstream are typically below the detection threshold (0.01 µg/L) of clinical assays. [2] Procalcitonin levels increase in response to pro-inflammatory stimuli, particularly those of bacterial origin. Pathologically, PCT is associated with both pathogen-associated and damage-associated molecular patterns. During a systemic inflammatory response triggered by infection, PCT is released into the bloodstream from various organs, including the thyroid, lungs, liver, pancreas, colon, and others. [3] It is therefore often classed as an acute phase reactant. The use of PCT, a useful biological index, contributes to differentiating bacterial infectious diseases,[4] especially with a high value in the diagnosis of sepsis.[5][6] Procalcitonin has an induction period of 4 to 12 hours and a half-life of 22 to 35 hours. Its levels do not significantly increase in viral or non-infectious inflammation. In viral infections, this is due to the production of interferon-gamma, a cellular response that inhibits the formation of procalcitonin.

During severe infections, the inflammatory cascade triggers a systemic response, causing procalcitonin levels in the blood to rise dramatically, with higher levels indicating more severe disease. Despite the elevated procalcitonin during infections, there is no corresponding increase in calcitonin or reduction in serum calcium levels. In normal homeostasis, pre-procalcitonin is initially synthesized by thyroid C cells. It is then converted into procalcitonin when a 25-amino acid signal sequence is cleaved by endopeptidases. The final product, calcitonin, a 32-amino acid hormone that regulates serum calcium, is formed through the action of the enzyme prohormone convertase. Under normal conditions, serum procalcitonin levels are very low, typically below 0.05 ng/mL. However, PCT synthesis can increase dramatically, by 100 to 1000 times, in response to endotoxins and pro-inflammatory cytokines such as interleukin (IL)-6, tumour necrosis factor (TNF)-alpha, and IL-1b, which stimulate various tissues. Extra-thyroidal synthesis of PCT has been identified in organs such as the liver, pancreas, kidneys, lungs, intestines, and within leukocytes.[3] However, it is important to note that in the absence of bacterial infection, PCT production in these tissues is suppressed. In contrast, cytokines like interferon-gamma (INF-gamma), released

during viral infections, reduce PCT levels, demonstrating another benefit of using PCT assays in distinguishing bacterial from viral infections.

In many hospitals across India, several inflammatory markers are routinely used to evaluate the prognosis of patients with acute pancreatitis. These include total and differential leukocyte counts, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). Additionally, various scoring systems, such as Ranson's criteria, Glasgow score, and the CT severity index, are employed to classify the severity of acute pancreatitis in patients.

Two commonly used CT scoring systems –CT severity index (CTSI), designed by Balthazar *et al*.,[7] and modified CT severity index (MCTSI), proposed by Mortele *et al*. [8] - require the use of intravenous (IV) contrast agents to determine the presence and extent of pancreatic necrosis, as well as inflammatory changes and local and/or extra pancreatic complications.

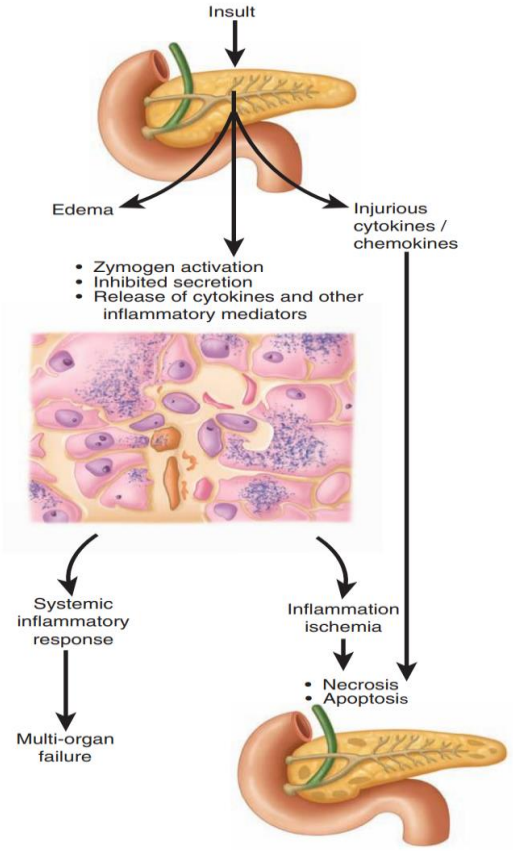
The CT Severity Index (CTSI) is a scoring system used to assess the severity of acute pancreatitis based on findings from a contrast-enhanced computed tomography (CT) scan. It combines the evaluation of pancreatic inflammation and necrosis to predict the prognosis and guide management. The CTSI includes the following components:

Pancreatic Inflammation:[9]
- **0 points:** Normal pancreas
- **1 point:** Intrinsic pancreatic abnormalities with or without inflammatory changes in peripancreatic fat
- **2 points:** Pancreatic or peripancreatic fluid collection or peripancreatic fat necrosis
- **3 points:** Single acute peripancreatic fluid collection
- **4 points:** Two or more acute peripancreatic fluid collections or presence of gas in or adjacent to the pancreas

Pancreatic Necrosis:[9]
- **0 points:** No necrosis
- **2 points:** ≤30% necrosis
- **4 points:** 30-50% necrosis
- **6 points:** >50% necrosis

The total CTSI score is calculated by adding the points from both the pancreatic inflammation and pancreatic necrosis categories. The scores range from 0 to 10, with higher scores indicating more severe disease and a worse prognosis.

Severity Classification:[9]
- **0-3:** Mild acute pancreatitis
- **4-6:** Moderate acute pancreatitis
- **7-10:** Severe acute pancreatitis



Table/Fig-1: Pathophysiology of acute pancreatitis

Acute pancreatitis is a nonbacterial inflammatory condition of the pancreas, triggered by the premature activation of digestive enzymes within the acinar cells, which can variably affect the gland itself, nearby tissues, and other organs. In severe cases, it can lead to necrosis of the pancreas and surrounding tissues, along with changes in serum enzymes like amylase and lipase. While most patients experience a mild, self-limiting form of the disease, about 20% develop multiple organ dysfunction syndrome (MODS), which is associated with a high mortality rate. Diagnosis of acute pancreatitis requires at least two of the following: abdominal pain, elevated pancreatic amylase and/or lipase levels to at least three times the normal upper limit, and characteristic findings on imaging.

Numerous studies have highlighted the role of plasma procalcitonin (PCT) in diagnosing sepsis, predicting the prognosis of severe acute pancreatitis, and serving as a marker following major surgeries. In addition to its use in sepsis diagnosis, PCT is valuable for monitoring the progression and severity of the systemic inflammatory response. However, certain non-infectious conditions can also lead to elevated PCT levels.

Aim and Objectives:

Aim

The Aim of the study is to analyze and compare the prognostic prediction of serum procalcitonin levels with CT severity index in acute pancreatitis.

Objectives
- Serum procalcitonin is an early and reliable prognostic

indicator in acute pancreatitis.
- To compare prognostic prediction of serum procalcitonin levels and CT severity index in mortality and morbidity of acute pancreatitis.
- Prediction of need for ICU care based on Serum Procalcitonin.

2. Materials and Methods

This Prospective observational study was conducted at Department of General Surgery, Kempegowda Institute of Medical Sciences and Research Centre, Bangalore, Karnataka, India from March 2021 to August 2022 done on a sample size of 51 patients. All patients gave informed written consent to participate in this study. The source of data was all those Patients diagnosed with Acute Pancreatitis, admitted in the Department of General Surgery, at KIMS Hospital and Research Center, Bangalore.

Inclusion Criteria:
All patients presenting with acute pancreatitis to the Emergency room.

Exclusion Criteria:
- History of trauma.
- Prolonged cardiogenic shock with impaired organ perfusion.
- Lung cancer or medullary carcinoma of the thyroid.

Protocol of the Procedure:
1) Inclusion and exclusion criteria were applied to all patients presenting with acute pancreatitis to the emergency medicine department of our hospital.
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) Plasma procalcitonin level determination was performed on the same serum sample drawn for other biochemical tests. The drawn blood was put in different vacutainers and labeled accordingly for the different tests.
5) Contrast enhanced Computed tomography of the abdomen and pelvis is done and CT severity index is calculated.
6) Descriptive and inferential statistical analysis was carried out on the data collected using SPSS 22.

Statistical Analysis:

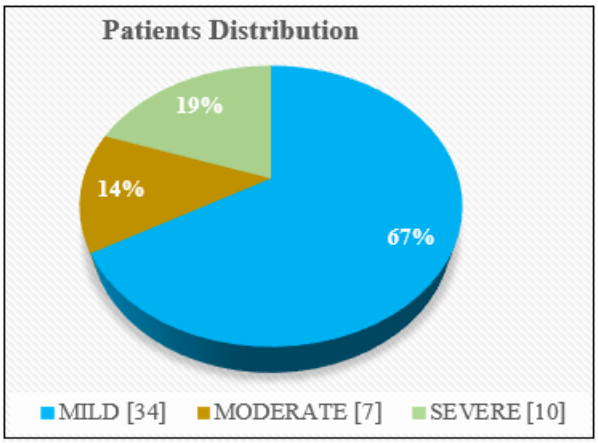
Statistical analysis is done using Statistical Package for Social Sciences [SPSS] for Windows Version 22.0 Released 2013. Armonk, NY: IBM Corp.

Descriptive Statistics:
Descriptive analysis of all the explanatory and outcome parameters will be done using frequency and proportions for categorical variables, whereas in Mean & SD for continuous variables.

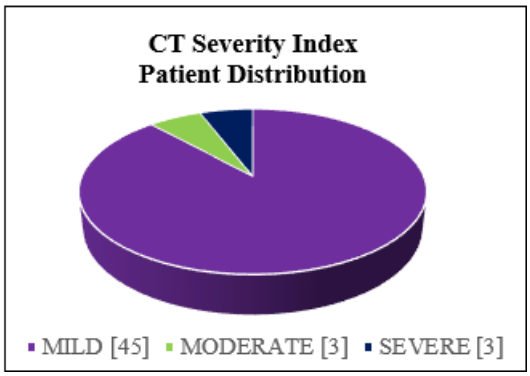
Inferential Statistics: Kruskal Wallis Test followed by Dunn's post hoc test was used to compare the mean serum procalcitonin levels based on the CT Severity scores among study patients. Mann Whitney Test was used to compare the mean Serum Procalcitonin levels based on the Survival status, Length of Hospital Stay and ICU Admission among study patients. Chi Square Test was used to compare the Survival status, ICU Admissions and Length of Hospital Stay based on the CT Severity among the study patients. ROC Curve analysis was used to predict the Mortality and Morbidity status among study patients based on serum procalcitonin levels and CT Severity scores among study patients. The level of significance was set at $p<0.05$.

3. Results

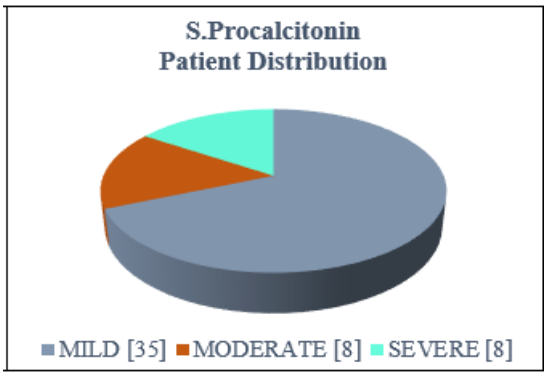
- Out of the total of 51 patients, all patients were males with a mean age of 42.29 years (range, 18-62 years). Twenty-one patients (41.1%) presented within 24 hours of onset of symptoms. Twelve patients (23.5 %) had recurrent pancreatitis, and 38 patients (74.5 %) gave history of consumption of alcohol within 72 hours prior to presentation and the rest with previous history of alcohol consumption. In all patients, alcohol was found to be the cause of acute pancreatitis.
- Table/Fig-2 shows distribution of patients diagnosed with acute pancreatitis into mild-67% (general wards), moderate-14% (HDU-High Dependency Unit) or severe-19% (ICU care) based on the general conditions of the patients by the attending doctors at the time of admissions.
- Table/Fig-3 shows distribution of patients according to CT severity index scoring system -CT severity index being -mild (0-3) 88%, moderate (4-6) 6%, severe (7-10) 6%.
- Table/Fig-4 shows patient distribution predicted with Serum Procalcitonin levels measured at the time of admissions-mild (<0.3ng/ml) 69%, moderate (0.3-0.5ng/ml)16%, severe (>0.5ng/ml)16%.The distribution predicted by serum procalcitonin levels at the time of admissions are very close to the actual distribution of the patients according to their general conditions when compared to distribution of patients predicted by CT severity index.



Table/Fig-2: Patients distribution



[Table/Fig-3]: CT Severity Index

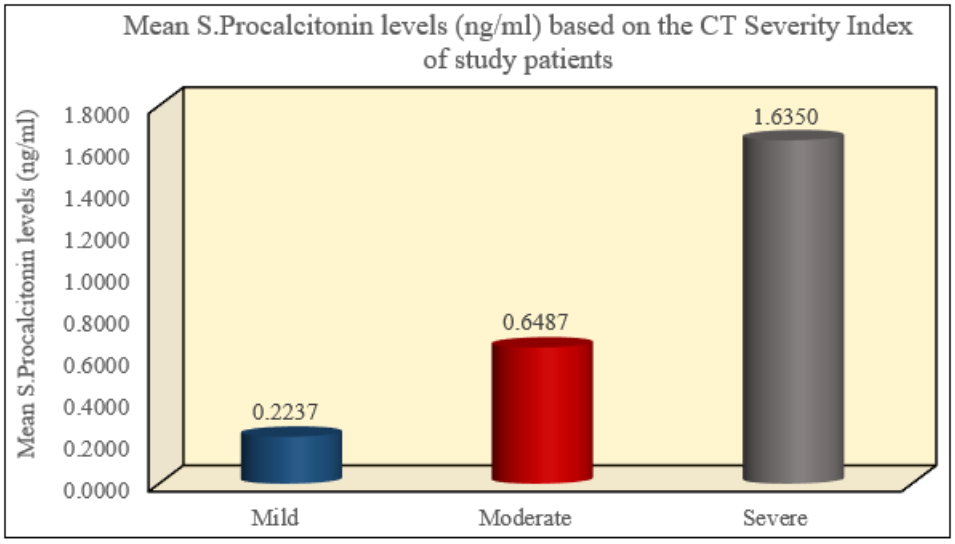


[Table/Fig-4]: S. Procalcitonin

Table/Fig-5: Comparison of mean S. Procalcitonin levels (ng/ml) based on the CT Severity Index of study patients using Kruskal Wallis Test followed by Dunn's Post hoc Test

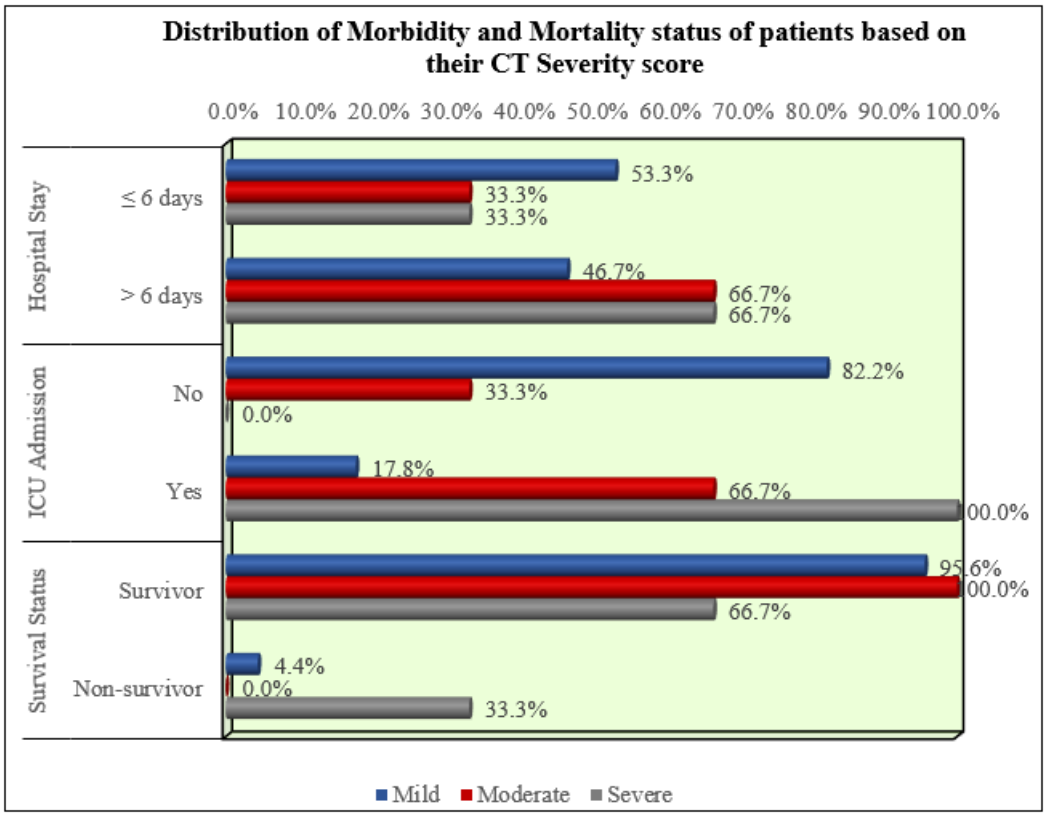
CT Severity	N	Mean	SD	Min	Max	p-value [a]	Sig. Diff	p-value [b]
Mild	45	0.2237	0.4249	0.002	2.120	<0.001*	Mi vs Mo	0.01*
Moderate	3	0.6487	0.2966	0.342	0.934		MI vs Se	0.009*
Severe	3	1.6350	1.5994	0.432	3.450		Mo vs Se	0.28

* - Statistically Significant
Note: a. Kruskal Wallis Test & b. Dunn's Post hoc Test
Mi – Mild. Mo – Moderate and Se – Severe



[Table/Fig-6]

- Table/Fig-5 and Table/Fig-6 showing comparison of mean S. Procalcitonin levels based on the CT Severity index of study patients using Kruskal Wallis test followed by Dunn's Post hoc Test showing statistically significant value.



Table/Fig-7

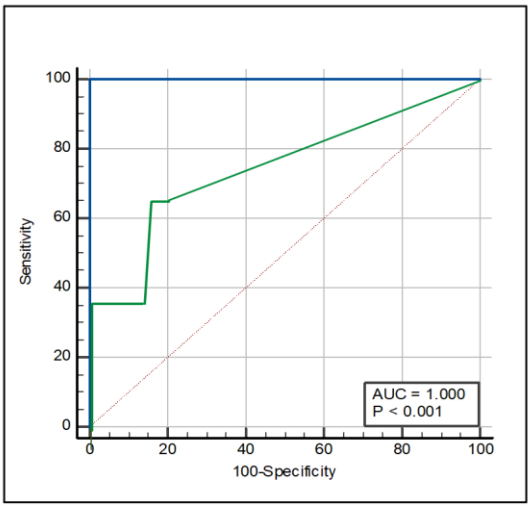
- Table/Fig 7 shows distribution of morbidity and mortality status of patients based on their CT severity score showing 100% of severe cases having ICU admission, with 66.7% of moderate cases having ICU admission, with both severe and moderate cases [66.7%] showing longer hospital stay of more than 6 days. Severe cases show a mortality rate of 33.3%.

Table/Fig-8: ROC Curve analysis for S. Procalcitonin levels in predicting the Mortality and Morbidity among study patients

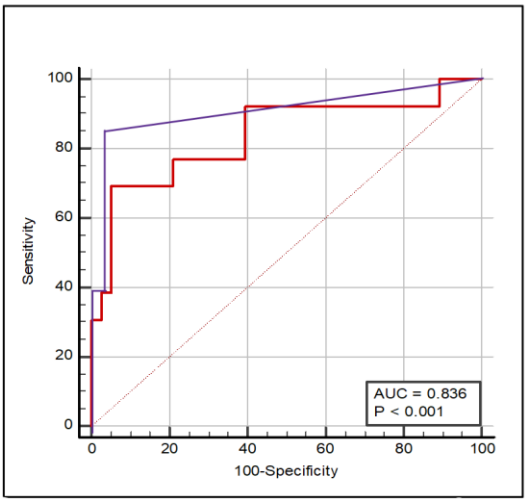
Variable	AUC	Std. Error	95% Conf. Interval		p-value	Cut off	Sn (%)	Sp (%)
			Lower	Upper				
Mortality	1.00	0.01	0.93	1.00	<0.001*	1.023	100.00	100.00
ICU Stay	0.83	0.08	0.71	0.93	<0.001*	0.321	69.23	94.74

Table/Fig-9: ROC Curve analysis for CT Severity Scores in predicting the Mortality and Morbidity among study patients

Variable	AUC	Std. Error	95% Conf. Interval		p-value	Cut off	Sn (%)	Sp (%)
			Lower	Upper				
Mortality	0.75	0.17	0.65	0.86	0.14	> 1	66.67	83.33
ICU Stay	0.91	0.06	0.80	0.97	<0.001*	> 0	84.62	97.37



Table/Fig-10: ROC curve for S.Procalcitonin Vs CT Severity Index in predicting mortality among study patients



Table/Fig-11: ROC curve for S.Procalcitonin Vs CT severity Index in predicting ICU admissions among study patients

- All patients who died (3) during the study was predicted as severe acute pancreatitis by serum procalcitonin levels but as moderate (1) and severe (2) by CT severity index which proves that serum Procalcitonin is a better predictor of mortality in patients with acute pancreatitis.
- Table/Fig-10 and Table/Fig-11 shows the ROC curve for S. procalcitonin with CT severity index in predicting mortality and ICU admissions among study patients. Using ROC curves, a cut off value of >0.5 ng/mL at admission for plasma procalcitonin was 100 % sensitive and 100% specific for predicting death in patients with pancreatitis when compared to CT severity index.

4. Discussion

- It is found that the CT severity index showed a positive correlation with the development of severe acute pancreatitis ($P < 0.001$).
- However, S. Procalcitonin was found to correlate better than RANSON score in predicting the progression of the disease to severe acute pancreatitis.
- A cut off value of 0.5 ng/mL at admission for S. Procalcitonin was 100 % sensitive and 100 % specific for predicting the progression to severe acute pancreatitis and mortality.
- Several studies have compared PCT to other inflammatory markers and have found that PCT is a good predictor of the severity of pancreatitis and the progression of the disease and development of organ failure. [11-18]
- A prospective international multicentric study by Bettina M et al.[19] assessed the role of plasma procalcitonin in the development of pancreatic infections and the overall prognosis of severe acute pancreatitis.in their study, they monitored both plasma procalcitonin 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.
- Plasma PCT is an excellent marker of sepsis. However, many non-infectious, proinflammatory states such as major trauma, drugs stimulating release of proinflammatory cytokines, prolonged cardiogenic shock, and prolonged organ hypoperfusion can all cause raised plasma levels of PCT. Pancreatitis, if severe, can also cause massive release of proinflammatory cytokines with a corresponding rise in plasma PCT levels. Studies have proved that this rise in plasma PCT values is a predictor of disease severity. A meta-analysis by Mofidi R et al. [20] Assessed the role of plasma procalcitonin in predicting the development of infected pancreatic necrosis and as well as the overall prognosis in noninfected severe acute pancreatitis. They concluded that plasma procalcitonin has a role in the management of both infected as well as noninfected severe acute pancreatitis. The meta-analysis also showed that the plasma PCT value within 24 h of admission can be used as a predictor of prognosis and subsequent values predict the development of infected pancreatic necrosis.

5. Conclusion

- Although Serum procalcitonin is not a specific marker of acute pancreatitis like serum lipase, Serum Procalcitonin at admission helps in predicting mortality and morbidity of patients with acute pancreatitis.
- In conclusion, both serum procalcitonin (S. Procalcitonin) levels and the CT severity index (CTSI) are valuable tools for assessing the severity of acute pancreatitis. The CTSI, through imaging, provides a detailed assessment of structural damage and complications such as necrosis and fluid collections, making it a reliable predictor of disease severity. However, serum procalcitonin levels have emerged as a more sensitive and dynamic biomarker, particularly in the early stages of the disease. S. Procalcitonin levels correlate well with systemic inflammation and are effective in predicting complications like organ failure and infections, offering a real-time indication of the inflammatory response.
- While both predictors play crucial roles in clinical

practice, serum procalcitonin has a distinct advantage in its ability to provide earlier and more consistent insights into disease severity, enabling timely interventions. Therefore, S. Procalcitonin may be considered a more effective predictor for guiding early management and monitoring the progression of acute pancreatitis.

References:

[1] Le Moullec JM, Jullienne A, Chenais J, et al. The complete sequence of human preprocalcitonin. FEBS Lett. 1984;167(1):93-7. doi:10.1016/0014-5793(84)80839-x.
[2] Maruna P, Nedelníková K, Gürlich R. Physiology and genetics of procalcitonin. Physiol Res. 2000;49(suppl 1).
[3] Müller B, White JC, Nylén ES, Snider RH, Becker KL, Habener JF. Ubiquitous expression of the calcitonin-I gene in multiple tissues in response to sepsis. J Clin Endocrinol Metab. 2001;86(1):396-404. doi:10.1210/jcem.86.1.7089.
[4] Schuetz P, Beishuizen A, Broyles M, et al. Procalcitonin (PCT)-guided antibiotic stewardship: an international experts consensus on optimized clinical use. Clin Chem Lab Med. 2019;57(9):1308-18. doi:10.1515/cclm-2018-1181.
[5] Diagnostics Advisory Committee. Procalcitonin testing for diagnosing and monitoring sepsis (Advia Centaur BRAHMS PCT Assay, BRAHMS PCT Sensitive Kryptor Assay, Elecsys BRAHMS PCT Assay, LIAISON BRAHMS PCT Assay and VIDAS BRAHMS PCT Assay); 2015.
[6] Müller B, Becker KL, Schächinger H, et al. Calcitonin precursors are reliable markers of sepsis in a medical intensive care unit. Crit Care Med. 2000;28(4):977-83. doi:10.1097/00003246-200004000-00011.
[7] Balthazar EJ, Robinson DL, Megibow AJ, Ranson JHC. Acute pancreatitis: value of CT in establishing prognosis. Radiology. 1990;174(2):331-6.
[8] Mortele KJ, Wiesner W, Intriere L, Shankar S, Zou KH, Kalantari BN. A modified CT severity index for evaluating acute pancreatitis: improved correlation with patient outcome. Am J Roentgenol. 2004;183(5):1261-5.
[9] Balthazar EJ, Robinson DL, Megibow AJ, Ranson JH. Acute pancreatitis: value of CT in establishing prognosis. Radiology. 1990;174(2):331-6. doi:10.1148/radiology.174.2.2296641.
[10] Weiss FU, Laemmerhirt F, Lerch MM. Acute pancreatitis: genetic risk and clinical implications. J Clin Med. 2021;10(2):190. doi:10.3390/jcm10020190.
[11] Kylänpää-Bäck ML, Takala A, Kemppainen EA, et al. Procalcitonin, soluble interleukin-2 receptor, and soluble E-selectin in predicting the severity of acute pancreatitis. Crit Care Med. 2001;29(1).
[12] Mándi Y, Farkas G, Takács T, Boda K, Lonovics J. Diagnostic relevance of procalcitonin, IL-6, and sICAM-1 in the prediction of infected necrosis in acute pancreatitis. Int J Pancreatol. 2000;28(1):41-9. doi:10.1385/IJGC:28:1:41.
[13] Modrau IS, Floyd AK, Thorlacius-Ussing O. The clinical value of procalcitonin in early assessment of acute pancreatitis. Am J Gastroenterol. 2005;100(7):1593-7. doi:10.1111/j.1572-0241.2005.41456.x.
[14] Mofidi R, Suttie SA, Patil PV, Ogston S, Parks RW. The value of procalcitonin at predicting the severity of acute pancreatitis and development of infected pancreatic necrosis: systematic review. Surgery. 2009;146(1):72-81. doi:10.1016/j.surg.2009.02.013.
[15] Muller C, Uhl W, Printzen G, et al. Role of procalcitonin and granulocyte colony stimulating factor in the early prediction of infected necrosis in severe acute pancreatitis. Gut. 2000;46(2):233-8. doi:10.1136/gut.46.2.233.
[16] Rau B, Steinbach G, Gansauge F, Mayer J, Grunert A, Beger H. The potential role of procalcitonin and interleukin 8 in the prediction of infected necrosis in acute pancreatitis. Gut. 1997;41(6):832-40. doi:10.1136/gut.41.6.832.
[17] Riché FC, Cholley BP, Laisné MJ, et al. Inflammatory cytokines, C reactive protein, and procalcitonin as early predictors of necrosis infection in acute necrotizing pancreatitis. Surgery. 2003;133(3):257-62. doi:10.1067/msy.2003.70.
[18] Riché FC, Cholley BP, Laisné MJ, et al. Inflammatory cytokines, C reactive protein, and procalcitonin as early predictors of necrosis infection in acute necrotizing pancreatitis. Surgery. 2003;133(3):257-62. doi:10.1067/msy.2003.70.
[19] Rau BM, Kemppainen EA, Gumbs AA, Buchler MW, Wegscheider K, Bassi C, et al. Early assessment of pancreatic infections and overall prognosis in severe acute pancreatitis by procalcitonin (PCT): a prospective international multicenter study. Ann Surg. 2007;245(5):745-54. doi:10.1097/01.sla.0000252443.22360.46.
[20] Kylänpää-Bäck ML, Takala A, Kemppainen E, Puolakkainen P, Haapiainen R, Repo H. Procalcitonin strip test in the early detection of severe acute pancreatitis. Br J Surg. 2001;88(2):222-7. doi:10.1046/j.1365-2168.2001.01673.x.