Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

Serum Creatinine: A Reliable Indicator for Pancreatic Necrosis in Acute Pancreatitis?

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Received: August 2016
Accepted: August 2016

ABSTRACT

Background: Necrotizing pancreatitis is one of the severe complications associated with acute pancreatitis. Serum creatinine has recently emerged as a reliable predictor of this severe complication associated with acute pancreatitis. **Aims and objectives:** The aim of this study is to evaluate the sensitivity and specificity of this simple biochemical marker in predicting the likelihood of developing pancreatic necrosis in any case of acute pancreatitis. **Methods:** A prospective study was carried out in Victoria Hospital, Bangalore over a period of two years and a total of 200 patients who presented with features suggestive of acute pancreatitis and further confirmed by computerized tomographic evaluation carried out within 96 hours of admission. Serum creatinine levels were documented at the time of admission, 24hrs and 48hrs after admission to notice if an elevation in serum creatinine corresponded with the development of pancreatic necrosis. **Results:** Out of the 200 test subjects, 26 (13%) patients developed pancreatic necrosis, which was confirmed by a contrast enhanced CT scan performed within 96 hours of admission into our centre. The sensitivity of serum creatinine alone in predicting the development of necrotizing pancreatitis was found to range between 75%-83% and the specificity varied between 71%-79% in our study. The positive predictive value ranges between 11%-23% with a negative predictive value ranging between 98%-99%. **Conclusion:** Serum creatinine though not highly sensitive is more specific and hence is a valuable simple and inexpensive biochemical parameter for predicting the development of pancreatic necrosis in cases of acute pancreatitis.

Keywords: Acute pancreatitis, computerized tomography, necrotizing pancreatitis, serum creatinine.

INTRODUCTION

Acute pancreatitis is an inflammatory condition of the glandular parenchyma leading to injury or destruction of the acinar components with little or no fibrosis and may or may not be associated with local and/or systemic complications. In the acute form the disease can be self- limiting with no further sequelae or result in catastrophic autodigestive activity resulting in complications such as pancreatic necrosis or multi organ failure with a high risk of mortality.[1]

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The worldwide incidence of acute pancreatitis ranges from 5 to 80/100,000 population with the highest incidence noted in Finland and US.[2] In 20% of the patients the attack is quite severe, resulting in an intense inflammatory response with a variety of local and systemic complications associated with significant morbidity and mortality. A crude mortality rate of 1/100,000 ranks it as the 14th most common fatal illness overall and the ninth most common cause of non cancer gastrointestinal death.

Necrotizing pancreatitis is a local complication, which may be associated with widespread systemic complications. It is seen in about 10%-15% of the patients and the mortality rates associated with this condition are as high as 27%-86%.[3-12] Studies have shown that pancreatic necrosis occurs within the first 2-4 days after an acute attack.[13]

Several approaches ranging from clinical estimation, biochemical markers and various imaging modalities to multivariable scoring systems involving all the above have been developed to estimate the severity of an acute episode, but a major setback of all these tools is their inability to assess the extent of injury to the pancreas and the peripancreatic tissue. Contrast enhanced CT scan is considered to be the ideal modality for diagnosing pancreatic necrosis.[14,15] Since contrast enhanced CT is an expensive diagnostic modality efforts are being made to identify simple biochemical investigations such as haematocrit, serum creatinine, blood urea nitrogen and serum glucose, which may reliably point towards the likelihood of developing pancreatic necrosis in cases of acute pancreatitis. Our study was

conducted with an intention of testing the accuracy of elevated serum creatinine values in predicting the development of necrotising pancreatitis.

MATERIALS AND METHODS

This was a prospective study conducted in the department of general surgery, Victoria hospital. The study included a total of 200 subjects. Patients who presented to the out- patient department or emergency centre of our institution with acute abdominal pain diagnosed to be secondary to an attack of acute pancreatitis, which was inferred by a threefold or more increase in serum amylase and lipase and further confirmed by contrast enhanced CT scan. Serum creatinine was estimated in all patients at pre set time frames i.e., at the time of admission and 24hrs and 48hrs after admission. All patients were made to undergo a contrast enhanced CT scan at any point of time between admission to 48hrs after. The sensitivity and specificity of serum creatinine in predicting the precense of pancreatic necrosis were evaluated based on the data collected. The positive and negative predictive values were also calculated utilizing the same data.

RESULTS

A total of 200 patients were included in the study. Serum creatinine level of ≥2mg/dl on admission or at 24 or 48hrs of admission was evaluated against the presence or absence of pancreatic necrosis confirmed by contrast enhanced CT scan.

At the time of admission (0hrs) a total of 45 patients had serum creatinine ≥2mg/dl out of which 4 patients had evidence of pancreatic necrosis on CECT. 2 patients had pancreatic necrosis, but their serum creatinine values was <2mg/dl, which remained so even on further follow up during the stay in the hospital.

A second sample of serum creatinine was sent at 24hrs for 194 patients without pancreatic necrosis previously and the results turned out to be as follows. 8 patients were proven to have pancreatic necrosis 24hrs after admission. 43 patients showed a serum creatinine value ≥2mg/dl out of which 5 had evidence of pancreatic necrosis on CECT. 3 patients, however continued to have serum creatinine values <2mg/dl during further follow up.

A third sample for serum creatinine estimation was sent at 48hrs after admission for 186 patients out of whom 12 had features suggestive of necrotizing pancreatitis on CECT. 6 out of these 12 patients had elevated serum creatinine and 34 who had elevated serum creatinine did not show any evidence of pancreatic necrosis.

Overall a total of 26(13%) patients developed pancreatic necrosis over a time period of 48hrs out of which 15(65%) had elevated serum creatinine above the cut-off point of 2mg/dl and 113 patients had serum creatinine levels of ≥2mg/dl but never progressed to develop pancreatic necrosis during their stay in our hospital.

The sensitivity of using serum creatinine as an indicator for predicting pancreatic necrosis was found to vary between 50%-66%, but the specificity was found to be higher and was calculated to be 78%-80% [Table 1]. The positive predictive value of using the same parameter was between 9%-15% and the negative predictive value in our study was found to be between 96%-98%.

Table 1: The sensitivity, specificity, positive/negative predictive value of using serum creatinine as an indicator for predicting pancreatic necrosis.

Time	Sensitivity	Specificity	Positive predictive value	Negative predictive value
0hrs	66%	78%	9%	99%
24hrs	62.5%	79%	12%	98%
48hrs	50%	80%	15%	96%

DISCUSSION

Acute pancreatitis on its own has turned out to be a major contributor to morbidity and mortality. The development of pancreatic necrosis in a pre-existing case of acute pancreatitis becomes a major contributor to this morbidity and mortality especially if the necrotic tissue undergoes infection.

Vascular compromise in the early phases of acute pancreatitis is believed to be the initiating factor in the development of pancreatic necrosis. Early prediction of the development of pancreatic necrosis will help in the better management of the patient and will compel the treating clinician to have a high degree of suspicion towards the development of more devastating complications associated with this condition such as development of infection in the necrotic tissue which may further lead to systemic complications such as multiple organ dysfunction or even death.

Fluid sequestration in the third spaces is one of the important steps in the pathophysiology of acute pancreatitis. Earlier blood urea nitrogen (BUN) which is one of the components of Ranson's criteria for assessing the severity of acute pancreatitis and serum creatinine were used to estimate the fluid status of the patient at the time of admission. BUN is sensitive to small changes in the intravascular volume, whereas severe volume depletion may cause reduction in the visceral blood flow leading to pancreatic necrosis, which may also affect the

kidneys which will be reflected in the form of elevated serum creatinine levels.

Several indicators such as haematocrit, BUN, C-reactive protein, α-2 macroglobulin, poly-morphonuclear elastase, human pancreas-specific protein/ procarboxypeptidase and serum macrophage migratory inhibitory factor have been evaluated as potential markers of pancreatic necrosis. Out of these C-reactive protein was considered to be the best predictor of pancreatic necrosis at 72hrs following admission.[16]

According to the Atlanta classification a serum creatinine of ≥2mg/dl is considered as the cut off point for acute renal failure. Hence in our study a value of ≥2mg/dl at the time of admission, 24hrs or 48hrs after admission was taken as significant and examined for the presence of pancreatic necrosis on contrast enhanced CT.

In our study a total of 26(13%) of the patients developed pancreatic necrosis out of whom 21 patients has serum creatinine ≥2mg/dl at varying points during their stay in the hospital. 5 patients, though they had evidence of pancreatic necrosis on contrast enhanced CT never had serum creatinine values ≥2mg/dl. The sensitivity of using serum creatinine as an indicator for pancreatic necrosis in our study was in the range of 50%-66%, but it proved to be highly specific with specificity ranging between 78%-80%. This is in consensus with the study conducted by Muddanna et.al[17] who conducted a study on 185 subjects and in those patients apart from serum creatinine, haematocrit, urea and nitrogen were also taken into consideration.

In the study conducted by Muddanna et. al[17] serum creatinine was sent at the time of admission to the hospital and a second sample was sent within 48hrs of admission. In 76(58.9%) of patients CECT was performed within 24hrs of admission and in 53 (41.1%) at a later time which was not specified in the study. Out of the 129 patients who were subjected to CECT 35 (27%) showed evidence of pancreatic necrosis. So utilizing this data, Muddana et.al have hypothesized that elevated serum creatinine can be used as a marker for pancreatic necrosis in acute pancreatitis. Similar to a study conducted by Muddanna et. al the sensitivity of elevated serum creatinine in predicting the development of pancreatic necrosis was on the lower end ranging between 50%-66% but the specifity was slightly higher between 78%-80% thereby supporting their hypothesis of using serum creatinine as a marker for predicting pancreatic necrosis.

Muddanna et. al[17] also have evaluated the accuracy of APACHE II and Ransons's scoring system which are considered to be the best predictors of severity of acute pancreatitis but are not routinely used in clinical practice . Although these methods show, better performance characteristics than single biochemical predictors like serum creatinine the authors have pointed out that many of the parameters in the above mentioned scoring systems cannot be routinely evaluated in all patients. Therefore, though serum creatinine has a lower sensitivity but a higher specificity and since it is an easily available biochemical marker, it can serve as an alternative to the more elaborate and expensive scoring systems. Therefore, any patient presenting with serum creatinine ≥2mg/dl should alert the clinician about the possibility of developing pancreatic necrosis and hence these patients have to be managed aggressively to prevent the development of this fatal complication. Furthermore, such patients should also be followed up closely after their discharge from the hospital.

Though serum creatinine has a very high specificity, it is too early to advocate the use of only serum creatinine as a marker for pancreatic necrosis. In our study, serum, creatinine was evaluated in all patients at 3 set time points so it does not take into account those patients who might have had fluctuation in serum creatinine in between those time frames and who had evidence of necrosis on CECT. Serum creatinine is also found to be increased in 4% of subjects after contrast administration for CECT[18] which was not taken into account in our study. In spite of all these drawbacks in our study, we would like to infer that serum creatinine can be utilized for predicting the development of pancreatic necrosis, however further studies are required to confirm the accuracy of this parameter.

CONCLUSION

The authors would like to conclude that though not highly sensitive serum creatinine, can be used to predict the development of pancreatic necrosis as early recognition of this complication is helpful in the optimal management of patients with acute pancreatitis.

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How to cite this article: Shashikala CK, Kavya T, Kagwad S. Serum Creatinine: A Reliable Indicator for Pancreatic Necrosis in Acute Pancreatitis? Ann. Int. Med. Den. Res. 2016; 2(6):SG15-SG18.

Source of Support: Nil, **Conflict of Interest:** None declared