

Clinical Implication of Increased Pancreatic Enzymes in ICU Patients

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Elevations in serum levels of pancreatic enzymes are usually in the range of 14–80% in intensive care unit (ICU) patients who have no prior pancreatic pathology.^{1,2} Although most of these patients do not develop clinical pancreatitis, pancreatic damage associated with elevated pancreatic enzymes is present. It is difficult to assess the clinical symptoms and signs of acute pancreatitis in ICU patients, especially in comatose, sedated, or mechanically ventilated patients. Serum amylase and lipase exceeding 3 times the upper normal limit are considered part of the criteria to diagnose acute pancreatitis.³ However, neither amylase nor lipase is specific for acute pancreatitis, and elevation of amylase and lipase does not correlate with the severity of pancreatitis. Imaging studies including abdominal ultrasonography and computed tomography (CT) are important tools to assess the etiology of elevated pancreatic enzymes. Imaging work-up for pancreatic damage is indicated for ICU patients with serum amylase or lipase levels > 3 times the upper normal limit.

What is the incidence of pancreatitis in ICU patients with increased serum amylase and lipase? In a recent issue of the *Journal of the Chinese Medical Association*, Lee et al⁴ reported their retrospective study that evaluated the clinical implication of increased serum levels of amylase and lipase in 89 neurosurgery ICU patients with abdominal symptoms and signs. Nearly half of these patients (48.3%) had elevated serum amylase and lipase. Nine out of 34 (26.5%) patients who were highly suspected to have acute pancreatitis (according to symptoms, signs, serum amylase and lipase levels > 3 and > 5 times, respectively, the upper normal limit), with peritoneal signs or fever of unknown origin, had imaging findings of pancreatitis on ultrasonography and/or CT. Only 1 of 9 patients had moderate pancreatitis; the others had mild pancreatitis. The exact causes of pancreatitis were not shown in the study. Manjuck et al⁵

found that imaging evidence of pancreatitis was present in 22% (11/50) of ICU patients with elevated lipase levels (above the upper normal limit). Denz et al² recently reported that 7 out of 20 (35%) ICU patients with serum lipase levels > 3 times the normal value had morphological alterations of the pancreas seen on contrast-enhanced CT.

Is increased serum pancreatic enzymes in ICU patients associated with higher mortality or longer ICU stay? Liu et al⁶ and Manjuck et al⁵ reported that ICU patients with elevated amylase and lipase levels did not have higher mortality, but had longer hospital or ICU stays compared to patients with normal amylase and lipase levels. On the contrary, Lee et al⁴ found that the mortality rate in patients with abnormal serum amylase and lipase levels was significantly higher than that in patients with normal amylase and lipase levels (39.5% vs. 17.4%, $p=0.033$), and elevation of pancreatic enzyme was not associated with longer ICU stay.

Chronic renal failure is commonly related to elevated serum amylase and lipase levels. The percentages of serum amylase and lipase greater than the upper normal limits in patients with chronic renal failure were 35.7% and 26.2%, respectively.⁷ In their study, Lee et al⁴ confirmed that renal failure may cause elevation of serum amylase and lipase. The percentage of renal failure (serum creatinine > 1.5 mg/dL) in patients with abnormal amylase and lipase levels was significantly higher than that in patients with normal amylase and lipase levels (27.9% vs. 8.7%, $p=0.026$).

The pathophysiology of pancreatic damage in general ICU or neurosurgery ICU patients is diverse. Several factors are proposed, including splanchnic hypoperfusion, bacterial translocation, elevated triglyceride levels, biliary sludge, head injury, acute stroke and drug adverse effects. Pancreatic damage associated with major surgery or shock has been well documented. The



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pancreas is highly susceptible to hypoperfusion and reperfusion injury. Nys et al⁸ reported a biphasic elevation of pancreatic enzymes in patients undergoing vascular surgery. The first peak occurred postoperatively and was related to ischemia, while the second peak developed 4–8 days after surgery and may be driven by inflammation.

Vitale et al⁹ showed that 23 out of 60 (38%) patients with severe head injury had increased total serum amylase levels. The source of hyperamylasemia was pancreatic isoamylase in 14, non-pancreatic isoamylase in 1, and mixed in 8 patients. However, no evidence of acute pancreatitis was found in these patients. In the report by Lee et al,⁴ patients with head injury or intracranial hemorrhage were found to have higher serum amylase and lipase levels compared with other neurosurgery ICU patients ($p=0.04$). Liu et al¹⁰ reported a rare case of acute pancreatitis that developed 10 hours after temporal lobectomy and hippocampotomy in a 23-year-old male patient with intractable seizure. Whether or not brain surgery affects the serum levels of pancreatic enzymes was not shown by Lee et al's study.⁴ They did not compare pancreatic enzyme levels before and after the surgical procedures.

The mechanism of the association between brain injury and acute pancreatitis or hyperamylasemia is unclear. Patients with acute traumatic brain injury are known to be hypermetabolic and have increased nutritional requirements.¹¹ Relative malnutrition and refeeding after malnutrition are known risk factors for the development of pancreatitis. In patients with head injury or acute stroke, the pancreas could also be affected by a failure of central regulation such as increased vagal activity, inappropriate cholecystokinin stimulation, or altered sympathetic tone.¹²

Propofol sedation was reported to cause higher incidence of hyperamylasemia in ICU patients (propofol 53% vs. non-propofol 14%, $p=0.0021$).¹³ The causal mechanism of propofol-induced pancreatitis is unclear. Hypertriglyceridemia is proposed as a putative mechanism. However, there was no significant elevation of pancreatic enzymes after propofol use in neurosurgery ICU patients in Lee et al's study.⁴

The incidence of exocrine pancreatic insufficiency in severely traumatized patients was reported to be 55.6% by measuring fecal elastase-1.¹⁴ Pancreatic exocrine dysfunction is related to the severity of illness in sepsis and ICU patients.¹⁵ Accordingly, pancreatic enzyme supplementation is necessary for these patients when enteral nutrition is tolerated.

In conclusion, elevation in serum amylase and lipase levels is common in ICU/neurosurgery ICU

patients. Acute pancreatitis is uncommon in these patients, and most pancreatitis observed is mild. Pancreatic enzyme supplementation may be necessary for ICU patients in whom feeding is tolerated. Whether or not elevated pancreatic enzymes is associated with higher mortality or longer ICU stay needs to be clarified with a large-scale study.

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