

Letter to the Editor

Pancreatic Enzymes Elevation and Emergency Setting: Pancreatitis or Not Pancreatitis? That is the Question

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Dear Editor,

Notwithstanding often no clinically evident acute pancreatitis findings are found, a serum pancreatic enzyme elevation is found in up to 80% of critically ill patients.^[1] In an emergency setting, in fact, the diagnosis of acute pancreatitis can be misleading due to various reasons, hence concomitant patients’ clinical conditions (e.g. hemodynamic instability, mechanical ventilation) and the establishment of rapidly evolving physiopathological mechanisms.

Does an enzyme increase justify the diagnosis of pancreatitis? Actually no. Although a three-time greater titer than upper limits represents one of the recognized diagnostic criteria, findings of hyperamylasemia and/or hyperlipasemia could lead to several interpretations, such as the evolution of severe acute pancreatitis, as defined by the Atlanta criteria, pancreatic complications in patients admitted for other pathologies or a mere biochemical increase in the absence of clinical-radiological signs attributable to pancreatic inflammation.

Furthermore, the enzymatic titer does not represent a prognostic factor or an index of progression to a necrotic or haemorrhagic state. Although, a diagnosis of acute pan-

creatitis at onset can be established on the basis of an enzymatic increase supported by suggestive clinical findings, the enzymatic dosage cannot be considered predictive of progression, as in case of the C-reactive protein. Furthermore, in the early stages of the disease, the extensive use of diagnostic radiologic investigations (<96 hours) has no role.^[2]

As reported by Weaver et al.,^[3] in a retrospective analysis including 192 emergency patients, 36.45% had hyperamylasemia but none met clinical or radiological criteria for acute pancreatitis. Furthermore, only 9.4% in this cohort was attributable to an increase in the pancreatic serum isoform. The authors therefore concluded by recommending caution in the dosage and interpretation of the titers of serum amylase in critically ill patients.

If on the one hand these evidences represent an explicit recommendation for a prompt and exhaustive nosological classification of hyperamylasemia that could mislead to an erroneous diagnosis, on the other they suggest the need for a critical review of the diagnostic criteria of acute pancreatitis where laboratory findings as far as clinical and radiological findings could lead to a reduced diagnostic power in critically ill patients.

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However, the same clinical criteria (abdominal pain, nausea and vomiting) are often misleading, as in case of patients with diabetic ketoacidosis where an elevation of the enzymatic titer is mainly attributable to a metabolic derangement such as dehydration, hyperglycemia and acidosis rather than to acute pancreatitis.^[4]

Organ failure, as in the case of end-stage chronic renal failure, could result in an enzymatic increase due to reduced glomerular excretion, hemodialysis effects or secondary hyperparathyroidism rather than pancreatic damage.^[5]

An alteration in host homeostasis as in case of polytrauma patients and, in particular, of traumatic brain injury due to the activation of central signalling pathways via vagal stimulation favouring an increased release of the pancreatic polypeptide has been reported.^[6] But, in general, all traumas and perfusion mismatches with an overwhelming shock can cause hyperamylasemia which represents an independent prognostic factor of incipient organ failure.^[7] In particular, in critically ill patients the need for mechanical ventilation would represent an epiphenomenon of the onset of a multiorgan failure, promoting a vicious circle where the exerted positive pressures and the altered venous return would favour a splanchnic venous stasis with ischemic microvascular effects.^[8]

Moreover, a relative increase in pancreatic enzymes has been shown to be a prognostic factor in infectious diseases, such as SARS-CoV2, where together with the onset of renal failure and oxygenation degradation indicate a progression towards a severe disease forms.^[9]

Finally, exogenous pharmacological causes for pancreatic enzymatic increase have been extensively described, as for hydrocortisone, amiodarone, dexamethasone or propofol administration.^[10]

Pancreatic serum enzymatic elevation in critically ill patients can be misleading for diagnosis of acute pancreatitis. A high awareness is therefore recommended in critically ill patients, where several pathophysiological mechanisms may justify this scenario.

Some limitations for a proper diagnostic approach could at least be mitigated by the assay of pancreatic enzyme isoforms or pancreatitis-associated proteins. However, we believe that a purely laboratory strategy is scarcely feasible due to the non-negligible aspects of universability, applicability and reproducibility for dosage.

Although ancestral evidence suggests a diagnostic role of the amylase P3 isoform and the lipase isoform,^[11] the assay that would demonstrate a better diagnostic power would be the serial comparison of lipase rather than amylase titers. On the other hand, it is also true that an approach

based only on the laboratory findings would lead to an unjustified downsizing of clinical and radiological criteria that should not be underestimated even when facing with emergency. For these reasons, concurrent pathophysiological effects should not be excluded a priori in an unstable patient (e.g. trauma, intestinal infarction, ketoacidosis or prolonged drug therapy such as in the case of heparins) in order to overcome diagnostic delays.^[12]

A certain skepticism and diagnostic doubt can therefore be raised in face of isolated hyperamylasemia or hyperlipasemia.

We believe that a comprehensive analytical step-up approach would be necessary. First of all, tests should rely on serial dosages over time. The persistence of the enzymatic elevation, the exclusion of metabolic causes (ketoacidosis, chronic end-stage renal failure), trauma or prolonged hospitalization (mechanical ventilation, pharmacological iatrogenic effect), would be an indication for a triphasic abdominal CT with the dual purpose for differential diagnostics (pancreatitis vs non-pancreatitis) and the investigation of collateral findings that may justify the laboratory findings.

A routine analysis is therefore not recommended but, in appropriate situations or with high clinical suspicion, hyperamylasemia and hyperlipasemia would suggest a rapid clinical deterioration.

Disclosures

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