EDITORIAL

Serum Cystatin C in Early Identification of Acute Kidney Injury in Acute Pancreatitis: Is It an Old Wine in a New Bottle?

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Keywords: Acute kidney injury, Acute pancreatitis, Biomarkers, Cystatin C.
Indian Journal of Critical Care Medicine (2020): 10.5005/jp-journals-10071-23579

Acute pancreatitis (AP) or acute inflammation of pancreas due to auto-digestion of pancreatic parenchyma and peripancreatic tissue is one of the most common gastroenterological disease. Predominantly, it is a mild and self-limiting disease without organ failure. However, if it is moderately severe or severe, it is usually associated with transient or persistent organ failure, respectively.[1] Acute kidney injury (AKI) is common in moderately severe and severe categories, usually as a part of multisystem organ failure and less commonly in isolation.[2]

Risk factors for AKI in patients with AP are mostly indirect and related to the release of inflammatory markers, relative or absolute hypovolemia, occurrence of hypotension, hypoxemia, and abdominal compartment syndrome secondary to ascites, ileus, or bowel edema.[2] Direct causation of AKI due to pancreatitis is yet to be elucidated. Acute kidney injury portends poor prognosis in AP with increased morbidity, ICU and hospital length of stay, resource use, increased cost, and reduced survival.[3]

Early mitigation of risk factors for AKI may help in reducing its occurrence and/or severity. The use of novel biomarkers of AKI may help in the early identification of AKI. Traditionally, serum creatinine and fall in urine output have been used to identify and grade AKI.[4] Potential concerns in using serum creatinine include its late rise, dependence on nonrenal factors, like age and lean body mass, its secretion by the tubules in addition to being filtered by the glomerulus, and many interferences with other endogenous substances.[5] The search for novel biomarkers of AKI in different settings has been ongoing.

Serum cystatin C is one such biomarker of kidney injury. It was discovered in 1961 and formally named in 1984.[6,7] It is a 13-kDa nonglycosylated, basic protein, with a polypeptide chain consisting of 120 amino acid residues synthesized by all nucleated cells at a constant rate. It is filtered freely by the glomerulus, completely reabsorbed and catabolized by the proximal convoluted tubules, and is not secreted by the renal tubules.[7]

Cystatin C is a unique biomarker and has multiple roles as it rises earlier than serum creatinine and can be used as a replacement of serum creatinine for the calculation of glomerular filtration rate (GFR).[5] It has been found to be a better marker of GFR as compared to creatinine.[6] It also has its utility in assessing the risk of death and cardiovascular events in elderly patients.[8] However, it does have limitations to its use in certain subsets of patients such as those with thyroid dysfunction, glucocorticoid therapy or with inflammation, where it may show aberrant values.[7] Regarding its analysis, currently, only two methods are commonly employed for its measurement in clinical studies: one is particle-enhanced nephelometric immunoassay (PENIA) and the other is particle-enhanced turbidimetric immunoassay (PETIA), the former is the recent one and also United States Food and Drug Administration (USFDA)-approved for measuring cystatin C.[5]

Patel et al.,[9] in their prospective observational study in this issue, evaluated the utility of baseline serum cystatin C for early identification of AKI in AP patients. They found area under receiver operating characteristic curve as 0.96, with a sensitivity of 92.06% at a specificity of 96.0% using the cut-off value of serum cystatin C as 32.32 ng/mL. Additionally, they also observed that the level of baseline serum cystatin C also correlated with stages of AKI quantitatively. Their study is remarkable for their cohort which was consisting of more than 60% of patients with moderately severe and severe AP. The method of detection used for serum cystatin C quantification was PENIA, which is a highly sensitive method. However, the cut-off value as observed by them seems different as compared to other studies.[10,11]

Although cystatin C has been discovered long back and appears to be a promising marker of renal injury, however, certain hindrances still exist in its wider clinical application including its cost, availability, and definition of normal value or range. The future research should be directed toward assessing the impact of early diagnosis of AKI using cystatin C on ICU outcomes.

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How to cite this article: Siddiqui SS. Serum Cystatin C in Early Identification of Acute Kidney Injury in Acute Pancreatitis: Is It an Old Wine in a New Bottle? Indian J Crit Care Med 2020;24(9):744–745.

Source of support: Nil

Conflict of interest: None

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