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Editorial

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Acute hyperglycemia facilitates contrast-induced nephropathy: independent risk marker in STEMI patients undergoing primary percutaneous coronary intervention

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Editorial

Diagnostic and therapeutic interventional procedures using iodinated radiographic contrast media may cause a relatively common complication called contrast-induced nephropathy (CIN).[1-4] CIN has a worse prognosis than acute renal failure not related to contrast media. CIN is the third most common cause of acute renal failure in hospitalized patients and it is associated with high short- and long-term morbidity and mortality.[5-12] CIN is defined as an increase in the serum creatinine level beginning within the first 24 h after contrast exposure and peaking in most patients up to 5 days after exposure (3-6). Most definitions have required a 0.5 to 1.0 mg/dl increase in the serum creatinine level and/or a rise in the serum creatinine level to 25% to 50% above baseline.[1-5] However, the Acute Kidney Injury Network has defined it as a rise in the serum creatinine level equal to or greater than 0.3 mg/dl or an increase in the serum creatinine level of 50% or more from baseline.[3]

The pathophysiology of CIN in acute hyperglycemia is poorly understood. Decreased glomerular filtration rate at baseline appears to be very important for its development. Two main factors are paramount, renal vasoconstriction and tubular injury.[3-5] Renal vasoconstriction is mediated by adenosine, endothelin, the high osmolality of some contrast agents, and blockade of endogenous vasodilators such as nitric oxide and local prostaglandins. Renal blood flow decreases up to 30% 2 h after contrast exposure and decreases up to 50% after 4 h. The association of volume depletion with reduced renal blood flow leads to increased viscosity, which predisposes to renal medullary hypoxia and ischemia.[3-6] Acute hyperglycemia may worsen this ischemic process since it may induce osmotic diuresis, resulting in volume depletion and dehydration and further increasing CIN risk and severity. This process may be facilitated by interstitial edema and may lead to loss of renal tubular cells. On the other hand, tubular injury is thought to result from a direct cytotoxic effect of iodinated contrast media, probably mediated by oxidative stress and the generation of reactive oxygen species. Stasis of contrast media in renal tubules may contribute to this phenomenon.[3-6]

The prevalence of CIN depends in part on a variety of patient-related and procedure-related factors.[11] The most important patient-related risk factor is pre-existing impairment of renal function. An estimated glomerular filtration rate of less than 60 ml/min/1.73 m2 may be accompanied with impaired renal vasodilation and reduced clearance of contrast media. These factors may facilitate the hemodynamic changes leading to decreased renal blood flow and tubular toxicity associated with use of these iodinated agents.[8-14] The presence of diabetes mellitus is a risk marker for developing CIN, especially in the case of diabetic nephropathy. Advanced aging also appears to be a risk factor for CIN. In addition, congestive heart failure and reduced left ventricular ejection fraction have been shown to be independent predictors of CIN, possibly related to impaired renal vasodilation.[14] Anemia, cirrhosis, and other hypovolemic entities characterized by low effective intravascular volume have also been identified as indicators of CIN.[15] Nephrotoxic drugs increase the sensitivity of the kidney to iodinated contrast media.[15]

On the other hand, procedure-related risk markers for CIN include the use of high-osmolar ionic contrast media, low-osmolar contrast media (compared with nonionic iso-osmolar contrast media), high volumes of contrast media, and multiple procedures requiring contrast media within 72 h.[3-6] Percutaneous coronary intervention (PCI) or peripheral artery intervention, coronary artery bypass surgery, and use of an intra-aortic balloon pump represent additional procedure-related risk markers.[12-18] The study of Khorshid H et al.,[17] in this issue of the Journal of Cardiology and Current Research investigated the association between admission acute hyperglycemia and the risk of subsequent (CIN) in patients with STEMI undergoing primary PCI. The authors studied 120 patients who presented with acute STEMI and were treated with primary PCI.

They divided their patients into 2 groups: Group A included 60 patients with acute hyperglycemia (blood glucose >198 mg/dl), and Group B included 60 patients without acute hyperglycemia on admission. Serum creatinine at the time of admission and daily for the following 5 days was measured. CIN was defined as an increase of ≥25% or an absolute increase of ≥0.5 mg/dl in serum creatinine level. The authors found a statistically significant difference regarding the incidence of CIN and need for dialysis between both groups, where CIN occurred in 23 (38.3%) patients, of which 9 patients required dialysis in group A, while in group B, CIN occurred in 8 (13.3%) patients, of which none needed dialysis ($P < 0.01$). In-hospital adverse events occurred more frequently in group A than group B. In Group A, 9 patients (15%) had acute pulmonary edema, cardiogenic shock and needed mechanical ventilation. On the other hand, in Group (B), 2 patients (3.3%) had acute pulmonary edema and 1 patient (1.7%) had cardiogenic shock and required mechanical ventilation ($P< 0.05$). Overall in-hospital mortality of the study population was 10% ($n = 6$) all of which were in group (A) ($P < 0.05$). They concluded that in patients undergoing primary PCI, acute hyperglycemia is associated with increased incidence of CIN as well as increased incidence of in-hospital adverse events and in-hospital mortality.[17]

Finn WF[19] reported an incidence of CIN that ranged from 3% to 31%. McCullough.[3] estimated that the overall incidence of CIN has decreased from approximately 15% to 7% over the past decade. They attributed this decreased incidence to a number of factors, namely, greater awareness of risk markers for the development of this syndrome, the development of less toxic contrast agents, and possibly the use of therapeutic interventions to reduce risk. In patients without risk markers, the reported incidence of CIN has been less than 2% in most studies.[3-5] The incidence remains low in patients with normal renal function despite the presence of diabetes mellitus. The incidence increases up to 11% in patients with mild to moderate renal insufficiency but rises to more than 40% in patients with volume depletion or heart failure.[3-6] CIN has been associated with an increased mortality risk in patients undergoing PCI. Studies of patients undergoing PCI, including those with acute myocardial infarction, have reported in-hospital mortality rates ranging from 6% to 31% in patients with CIN.[3-8] If the PCI patient requires dialysis, the In-hospital mortality rates range from 22% to 36%.[8, 9]

It was demonstrated that pre-procedural blood glucose levels are a risk marker for CIN in patients without diabetes mellitus with acute myocardial infarction who undergo primary PCI.[16]. However, this finding was not observed in patients with diabetes mellitus in this study, perhaps because of higher baseline risk for CIN. Hyperglycemia in patients without diabetes mellitus is commonly observed in critically ill patients and occurs in more than 40% of patients without diabetes with acute myocardial infarction.[18] The etiology of hyperglycemia in this setting is uncertain but may relate in part to stress-related neurohormonal alterations, including stimulation of catecholamines, activation of the renin-angiotensin-aldosterone system, and expression of various cytokines. It was also postulated that hyperglycemia occurs because of insulin resistance.[18] In addition, admission fasting blood glucose was demonstrated to be an independent predictor of CIN in patients with the metabolic syndrome.[15]

Acute hyperglycemia is known to be associated with several mechanisms and adverse effects that contribute to poor outcome in patients with acute myocardial infarction. These mechanisms include increased oxidative stress, increased cytokine activation, prothrombotic effects, enhanced platelet activation, inflammatory response, endothelial dysfunction and impaired microcirculatory function as manifested by post-PCI no-reflow and impaired ischemic preconditioning.[19-26] Several studies have demonstrated that acute hyperglycemia, regardless of the diabetic state, is a powerful predictor of mortality, larger infarct size and increased risk of cardiovascular complications in patients with myocardial infarction.[27-34] Stranders I et al.[33] demonstrated that for every 18-mg/dL increase in glucose level, there is a 4% increase in mortality in non-diabetic patients presenting with myocardial infarction (33).

We agree with Khorshid H et al.,[17] in their assumption that being admission glucose level measurement readily available for all patients presenting with STEMI, this variable could be incorporated into risk calculation models for identification of patients at risk for development of CIN after primary PCI. On the other hand, it is relevant and necessary to further investigate if admission hyperglycemia serves as a risk marker for CIN in patients out of the context of acute coronary syndrome who receive iodinated contrast media during diagnostic coronary angiography.

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Conflicts of interest

There were no financial interest or conflict of interest.

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