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Editorial

Radiocontrast-induced nephropathy in patients with liver cirrhosis and chronic kidney disease

Radiocontrast-induced nephropathy (RCIN) represents one of the leading causes of hospital-acquired acute kidney injury (AKI) worldwide, and due to an increase in the number of procedures that use contrast agents for various diagnostic and therapeutic purposes, especially in high-risk patients, the incidence of RCIN has been reported to be up to 25% in patients with chronic kidney disease (CKD) [1,2]. Although the typical clinical course of CIN is known to be characterized by an early peak of serum creatinine concentration in 3–5 days, returning to baseline within 7 days, it can also be associated with a more severe and prolonged course of AKI in patients with CKD, with a possible deleterious impact on the progression of CKD [3–5].

The pathogenesis of RCIN includes a combination of renal ischemia, direct and indirect tubule toxicity mediated by reactive oxygen species, and tubule obstruction. Therefore, various drugs and clinical conditions that can reduce renal plasma flow or impair renal autoregulatory function might serve as risk factors; these may include decreased true or effective circulating volume, diabetes mellitus, presence of CKD, shock, or the use of nonsteroidal anti-inflammatory drugs. However, despite a better understanding of the pathogenesis, there are no specific treatment strategies, and in clinical practice hydration with isotonic sodium chloride or sodium bicarbonate for the purpose of maintaining urine flow remains a mainstay in prevention.

Cirrhosis of the liver is a condition that is characterized by the replacement of liver tissue by fibrosis, scar tissue, and regenerative nodules, which ultimately leads to a loss of liver function. The presence of acute or chronic renal complications is common in these patients, and is known to be associated with poorer outcome. Cirrhotic patients are likely to be prone to the development of an acute deterioration of kidney function, due to the presence of a reduced effective circulating volume, which is often aggravated by the use of diuretics, large-volume paracentesis, or gastrointestinal bleeding [6]. Furthermore, the presence of hyperaldosteronism, altered renal hemodynamics, or infection can escalate susceptibility to the development of AKI. Although the most common form of renal complications in cirrhotic patients is hemodynamically mediated functional impairment, the concomitant presence of CKD is also common. However, in diagnosing CKD or AKI, serum creatinine concentration is known to be more inaccurate, especially in decompensated cirrhotic patients, possibly due to a reduced production of creatinine from creatine in the liver, and also due to the concurrent presence of muscle wasting. Therefore, the use of creatinine-based estimated glomerular filtration rate (eGFR) has more limitations in these patients.

With advances in antiviral and supportive care, the longevity of cirrhotic patients has increased, and it is expected that the use of radiocontrast for computed tomography (CT) scanning or angiography with the purpose of early recognition and proper treatment of hepatocellular carcinoma or for other co-morbid conditions will rise. Additionally, both a reduced effective circulating volume and altered renal hemodynamics per se in cirrhotic patients are expected to increase the incidence of RCIN. However, whether liver cirrhosis itself portends an added risk factor in the development of RCIN, or whether preventive strategies such as hydration with normal saline or sodium bicarbonate could be safely carried out in these patients, has not been thoroughly investigated.

In this issue of *Kidney Research and Clinical Practice*, Choi et al evaluated the incidence of RCIN in patients with liver cirrhosis and CKD (eGFR ≤ 60 mL/min/1.73 m^2). They also tested the effect of intravenous albumin for prophylaxis of RCIN. By retrospectively comparing the incidence of RCIN in 81 patients, defined as $\geq 25\%$ or ≥ 0.5 mg/dl rise in serum creatinine concentration measured 2–5 days after CT scanning, they first demonstrated that the overall incidence of RCIN in patients with liver cirrhosis and CKD who received RCIN prophylaxis protocols that included N-acetylcysteine with sodium bicarbonate or albumin was relatively low (3.7%). They also showed that there was no difference in the incidence of RCIN between sodium bicarbonate and albumin prophylaxis. As the authors quoted, only three studies so far have examined the incidence of RCIN in patients with liver cirrhosis, and their results have been controversial [7–9].

Although the exact reasons for the discrepancy in the results between the studies are not known, this current study by Choi et al has strengths in that it examined the incidence of RCIN in patients with combined liver cirrhosis and CKD for the first time. In addition, despite several limitations of this study, it is noteworthy for its observation that the overall incidence of RCIN in patients with combined liver cirrhosis and CKD who underwent prophylactic procedures was low.

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However, due to the absence of a control group who did not receive prophylaxis, it remains unclear whether this relatively low incidence of RCIN originated from the prophylaxis. Additionally, because the incidence of RCIN in patients with combined liver cirrhosis and CKD was not compared with that in patients with CKD alone, we cannot tell from this study whether liver cirrhosis itself might further increase the risk of RCIN.

In assessing the risk factors for the development of RCIN in these patients, only the presence of ascites was found to be a risk factor, but diabetes mellitus and lower eGFR, well-known traditional risk factors for RCIN, were not associated with the development of RCIN. Although the presence of ascites in cirrhotic patients has also been demonstrated to be an independent risk factor for RCIN in another study by Lohida et.al, caution should be taken in drawing them same conclusion from this study because, due to a very limited number of RCIN cases, the number of patients was too small to convincingly define the risk factors.

The other purpose of this study was to examine the effect of albumin prophylaxis on the prevention of RCIN. Albumin is currently used as a volume expander in large-volume paracentesis or as a bridge therapy to liver transplantation in hepatorenal syndrome. Albumin infusion, instead of isotonic sodium chloride or sodium bicarbonate infusion, may have theoretical advantages in terms of a more effective expansion of intravascular volume or through its possible antioxidant effect. Two out of the 38 patients who received albumin prophylaxis developed RCIN (5.3%), compared with 2.3% (1/43) in the sodium bicarbonate group, and this difference was not statistically significant. However, as mentioned earlier, because the number of RCIN cases in both groups was too small, no meaningful conclusion can be drawn regarding the effect of albumin prophylaxis. Furthermore, significant differences in the baseline characteristics, such as a more severe degree of liver dysfunction, which was represented by a higher Child–Pugh class or a higher prevalence of ascites in the albumin prophylaxis group, make data interpretation more complicated. The authors demonstrated that patients in the albumin prophylaxis group showed a lower degree of weight gain after a CT scan (0.1 ± 0.9 vs 0.5 ± 0.7 kg). However, we have to consider whether the possible clinical benefit of lesser weight gain, of about 0.4 kg, in the albumin prophylaxis group indeed outweighed the possible negative effects of albumin infusion—possible viral transmission despite a low incidence and also higher economic costs.

The concomitant presence of CKD in cirrhotic patients is increasingly recognized in clinical practice, and episodes of AKI, including RCIN, in these patients might be associated with a faster progression of CKD. Although liver cirrhosis itself is often considered to be a risk factor for RCIN, the incidence, risk factors, or effects of conventional hydration strategies in these patients are largely unknown. Recognition of the exact incidence and risk factors in these particular patient populations is of great importance in establishing proper preventive strategies, potentially having a positive impact on patients' outcome.

Recently, a new working party, which consists of members of the Acute Dialysis Quality Initiative and International Ascites Club, proposed a newer classification system for AKI in cirrhotic patients [10]. Only an increase in serum creatinine concentration of 50% from the baseline or 0.3 mg/dl or more during the 48 hours was chosen, excluding urinary output criteria owing to a possible lack of reliability of the urine output in patients with refractory ascites. Based on this newer classification system, large-scale, multicenter, prospective clinical trials are urgently needed to develop and validate the risk quantification, and also establish preventive strategies for RCIN in patients with liver cirrhosis.

Conflict of interest

None.

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