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Save the Brain First: CTA and Mechanical Thrombectomy in Patients at Risk for Contrast-Induced Nephropathy

Stroke is one of the most common diseases affecting 800,000 Americans each year. It ranks fourth among all-cause mortality in the United States.[1] When patients present with stroke-like symptoms, the current American Heart Association/American Stroke Association (AHA/ASA) guidelines recommend an immediate non-contrast CT of the head. If large-vessel occlusion is suspected, CTA or MRA should be performed to assess the vascular anatomy and plan for endovascular therapy. If the patient is a candidate for mechanical thrombectomy, cerebral angiography is performed.[2] Both CTA and mechanical thrombectomy will subject patients to intravenous contrast.

The concern for exposing patients to a large amount of intravenous contrast is the development of contrast-induced nephropathy (CIN). It is defined as an increase in the plasma creatinine level of 0.5 mg/dL or >25% increase from the baseline within 2–5 days of contrast exposure without any other attributable cause.[3] Multiple risk factors can predispose patients to CIN. Tsai et al[4] have shown that severe chronic kidney disease (CKD), defined as an estimated glomerular filtration rate (eGFR) of <30 mL/min/1.72m^2, was the most significant risk factor for the development of CIN. Most important, acute kidney injury (AKI) in patients with stroke has been associated with an increased risk of in-hospital mortality.[5] Therefore, CIN is a relevant clinical entity and needs to be managed appropriately.

When the initial head CT is negative for bleeding, the question arises as to when and whether the patient should undergo CTA and subsequent revascularization. The current AHA/ASA guidelines recommend proceeding with CTA in patients without a history of renal disease.[2] However, for patients with a history of CKD, there is no current consensus guideline. Therefore, we believe the article by Myung et al[6] has shed valuable light on the risk-stratification and clinical decision-making for this patient population.

The authors conducted a retrospective observational study examining the relationship between CIN and baseline renal function in a large cohort involving 601 patients undergoing CTA and cerebral angiography. The authors demonstrated that patients with severe CKD (eGFR of <30 mL/min/1.73 m^2) were at a higher risk of CIN ($P < .001$). The CIN incidence rate was 12.5% in all patients with CKD and 46.6% in patients with severe CKD. Furthermore, the cutoff eGFR value for an increased CIN risk was found to be 43 mL/min/1.73 m^2. Most important, there was no reported mortality in the patients with CIN. Only 5 patients underwent dialysis, and all patients fully recovered renal function within 4 days. Due to its retrospective observational nature, in this study, a causal relationship could not be established between intravenous contrast and CIN. Furthermore, the absolute CIN incidence rate in patients with CKD was low. Patients with severe CKD were at an increased risk of CIN. However, the clinical consequence is not necessarily significant because all patients recovered successfully after a short course of dialysis and no in-hospital mortality was reported. The authors concluded that neurological interventions should take precedence over concerns of renal injury. However, the understanding of CIN risk factors may help guide individualized renal protective therapy.

Similar to the authors' conclusion, it is absolutely reasonable to proceed with endovascular therapy regardless of the patient's baseline renal function. It is important to proceed with neurovascular interventions before the creatinine level is drawn to avoid a prolonged time to intervention.

First, there is a growing body of evidence showing that intravenous contrast may not cause CIN, particularly in patients with unremarkable baseline renal function. A 2013 systematic review and meta-analysis showed no difference in the rate of AKI between patients with and without contrast exposure.[7] In 2017, a systematic review of 14 studies revealed that CTA and CT perfusion scans were not significantly associated with an increased risk of developing AKI.[8] Furthermore, Lima et al[9] have shown that there was no difference in the AKI rate between patients undergoing CTA and thrombectomy and those without any contrast exposure. Other studies have found similar results.[10,11] Of course, the major critique is that high-risk patients might be scanned much less frequently than the generally healthy patient population owing to the concern for CIN. Therefore, the CIN incidence in the contrast-exposure group may have been erroneously low. On the other hand, stroke may disrupt neurohormonal pathways and may contribute to the development of AKI.[12]

Second, although CIN has been reported to range as high as 20%–30% in the high-risk renal population, the true incidence rate may be much lower. A 2013 study showed that 9%–11% of the at-

risk patients developed postcontrast AKI.[13] A 2017 meta-analysis showed that 2.3% of the patients with CKD undergoing CTA were affected by AKI.[7] Similarly, other studies have found that the absolute CIN rate was low in at-risk patients.[14] The often-quoted high CIN incidence rate was partially due to the use of older hyperosmolar contrast agents, which have been associated with an increased risk of CIN.[15] Furthermore, the incidence of CIN in patients undergoing neurovascular therapy is also low. In a study including 185 high-risk patients undergoing cerebral angiography and mechanical thrombectomy, only 1 patient developed CIN.[16] Similarly, Loh et al[17] found that 3 of 99 patients undergoing endovascular therapy had AKI. In a more recent study, 12 of 93 patients with CKD developed AKI after CTA and thrombectomy, though CKD was not an independent risk factor for AKI in this study.[18]

Last, although CIN has been associated with an increased in-hospital mortality, the true clinical significance of CIN may also be overestimated. It is plausible that CIN is a surrogate marker of rather than a causative factor for worse clinical outcome. For example, the degree of renal impairment is typically minor. McDonald et al[7] have shown that the rate of dialysis was 0.3% in patients developing CIN. Furthermore, effort to reduce renal impairment does not improve the overall mortality rate. Coca et al[19] have shown that reducing the AKI rate by >50% did not reduce the risk of long-term mortality.

Currently, there is no prospective, randomized controlled trial comparing the risk of AKI in patients with CKD with and without contrast exposure. Therefore, no true causal relationship can be established. However, based on existing literature, there is evidence indicating that intravascular contrast does not cause CIN. Furthermore, the absolute rate of CIN remains low, and the clinical significance is unclear. It is more likely that CIN is a surrogate marker reflecting critical illness and multimorbidity rather than a factor determining patient outcome. In that case, assessing a patient's renal function before CTA and mechanical thrombectomy may have no clinical benefit from a renal-protective perspective, even for patients with CKD. Furthermore, each minute wasted on obtaining laboratory data may cost patients 1.9 million neurons in the stroke population.[20] Therefore, it is prudent to proceed with CTA and mechanical thrombectomy on the basis of neurologic status regardless of the patient's renal function. In the future, prospective, randomized controlled trials for patients with severe CKD may be considered, but ethically, it will be difficult not to treat patients if they are otherwise candidates for mechanical thrombectomy. Time is indeed brain, and brain should be saved first.

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