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REVIEW

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Contrast Nephropathy Review

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Abstract

Contrast-induced nephropathy (CIN) is a common cause of acute kidney dysfunction. It is necessary to identify at-risk patients at early stages to implement preventive strategies to decrease the incidence of this nephropathy. However, mechanisms of CIN have not fully explained yet. Most predictive models for contrast-induced nephropathy in clinical use have modest ability and are only relevant to patients receiving contrast for coronary angiography. Further research is needed to develop models that can better inform patient-centred decision making, as well as improve the use of prevention strategies for contrast-induced nephropathy.

Keywords: *Nephropathy, Contrast,Coronary intervention*

Introduction

Contrast-İnduced Nephropathy (CIN) refers to the reversible form of acute renal failure that results in secondary to contrast exposure. CIN is one of the essential post-operative adverse events after cardiac procedures. The incidence of CIN has been calculated to be > 2% in the general population. Still, in high-risk patients, i.e., diabetic patients, subjects with a history of congestive heart failure, chronic renal impairment, and older age, the incidence has been considered to be > 20% to 30% [1]. The definition of CIN comprises free (≥ 0.5 mg/dl) or relative increase (≥ 25%) in serum creatinine value at 48-72 h after exposure to a contrast agent compared to baseline serum creatinine values. At the same time, alternative explanations for renal impairment have been excluded [2,3]. CIN is a severe complication of Percutaneous Coronary İntervention (PCI). It is associated with considerably increased morbidity, including the need for short-term hemodialysis, extended hospitalisation, and permanent impairment of renal function [4]. Most importantly, the development of CIN is independently associated with increased in-hospital and long-term mortality [5].

Clinical Assesment

Harjai, et al. [3] categorized, contrast nephropathy as grade 0 (serum creatinine increase < 25% above baseline and < 0.5 mg/dL above baseline), grade 1 (serum creatinine increase ≥ 25% above baseline and < 0.5 mg/dL above baseline), or grade 2 (serum creatinine increase ≥ 0.5 mg/dL above baseline).

Mehran, et al. have reported a risk score for the prediction of CIN after the percutaneous coronary intervention [6]. Their suggested risk scores include hypotension (5 points, if systolic blood pressure < 80 mm Hg for at least 1 hour requiring inotropic support), use of intra-aortic balloon pump (5 points), congestive heart failure (5 points, if class III/IV by New York Heart Association classification or history of pulmonary oedema), age (4 points, if > 75 years), anaemia (3 points if hematocrit < 39% for men and < 36% for women), diabetes mellitus (3 points), contrast media volume (1 point per 100 mL), estimated glomerular filtration rate (eGFR); 2 points, if eGFR 60 to 40; 4 points if eGFR 40 to 20; 6 points if eGFR < 20. A risk score of > 6, 6 to 10, 11 to 16, and > 16 indicates a risk for CIN of 7.5%, 14%, 26%, and 57%, respectively.

Pathophysiology

The precise mechanisms of CIN have not been explained in details. Several factors have thought to be related to the pathogenesis of CIN, for example, hemodynamic changes of renal blood flow, which causes hypoxia in the renal medulla, the direct toxic effect of the contrast media on renal cells [7]. Furthermore, contrast agents have direct toxic effects on kidney tubular cells, inducing vacuolization, change in mitochondrial function, and even apoptosis [8]. Diabetes mellitus (type 1 and type 2) and impaired kidney function are considered as significant risk factors for CIN. In high-risk patients, different levels of GFR can be regarded as a risk factor too. The highest risk is associated with GFR of less than 30 mL/min; the lowest risk, with GFR levels of 60 mL/min or higher, except for patients with diabetes [9]. Additionally, diabetic subjects with normal GFR have increased risk of CIN because of endothelial dysfunction of the renal vessels, resulting in the suppressed tonic influence of nitric oxide [10].

Treatment

Studies suggest that intravenous hydration is the most effective strategy to prevent CIN [11]. The volume of contrast media and the frequency of administration should be minimised, to ensure satisfactory image quality. Sodium bicarbonate and N-acetylcysteine are considered as two strategies which are recommended to prevent an acidic environment and formation of free radicals in the renal tubules [12]. Compared with an infusion of normal saline alone, administration of N-acetylcysteine in conjunction with injections

of normal saline significantly decreased the risk for CIN [13]. Ascorbic acid, theophylline, fenoldopam, and calcium antagonists, and periprocedural hemofiltration have been recommended to prevent CIN too [14].

Discussions

The true incidence of CIN is challenging to assess because of the differences in the definition of contrast agent nephropathy across the various studies, the proportion of high-risk patients, the types of contrast media used, and the use of preventive measures. These variables should all be considered in future model development. However, prognostic factor selection and measurement were poorly described across most studies. However, the scope of CIN is vast. Few other studies found that the female gender was an independent predictor of CIN development after PCI and a marker of increased one-year mortality after CIN in patients with no underlying chronic kidney disease [15,16]. Lautin, et al. where diabetes patients with baseline normal renal function had a higher risk of developing CIN [17]. Rihal, et al. observed that when renal function is mildly impaired, the risk of CIN in people with diabetes was 4.1%, about twice that in patients without diabetes [5]. Drug treatments such as inhibitors of the renin-angiotensin-aldosterone system and diuretic agents could increase susceptibility to contrast-induced nephropathy through alterations in kidney haemodynamics [18].

A retrospective analysis of data from the Mayo Clinic PCI Registry also revealed significantly higher short-term mortality with CIN. Of the 7586 patients undergoing PCI, 254 patients (3.3%) experienced CIN, and the in-hospital mortality rate for these patients was 22% compared with a rate of 1.4% for the patients who did not develop CIN ($p < 0.0001$) [19]. In the same study, it was also found that people with diabetes more commonly developed CIN. Unlike Mayo clinic registry, the present study showed higher CIN without any mortality as compared to previous findings from Mayo clinic as well as from Victor's observation where 0.5% of patients died due to CIN [20].

The risk of contrast-induced nephropathy associated with intravenous, contrast-enhanced CT procedures is not rare, occurring in 11% of a low-risk population [21]. Besides, the pathophysiological mechanism of contrast-induced nephropathy related to contrast-enhanced CT procedures could differ from that associated with coronary angiography procedures [22]. For example, in intravenous procedures involving contrast-enhanced CT, a large volume of intravenous contrast is often injected within 10 to 20 seconds compared with small intra arterial injections of contrast occurring over minutes in coronary procedures. As such, predictive models for variation induced nephropathy derived from patients undergoing coronary angiography might not be generalisable to individuals suffering from intravenous contrast-enhanced CT procedures or CT angiography.

Currently, there are no definitively effective strategies for the prevention or treatment of contrast-induced nephropathy [23,24]. The provision of intravenous fluids (containing saline or bicarbonate) and N-acetyl cysteine have been extensively studied for prophylaxis; however, no conclusion on efficacy has been reached despite multiple prospective trials and several meta-analyses [25].

Conclusions

Although higher-performing models usually include pre-existing chronic kidney disease, age, diabetes, heart failure or impaired ejection fraction, and hypotension or shock, most have the limited predictive ability when validated externally and are not relevant to individuals receiving intravenous contrast or non-coronary angiography. Given the increasing incidence of contrast-induced nephropathy and the many clinical applications of risk prediction, it is necessary to build on current models to develop a clinically useful and generalisable prediction model for the disorder that can improve clinical decision making and patient outcomes. A crucial step to reduce CIN is to identify patients at risk of CIN.

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