

Contrast-induced acute kidney injury/contrast-induced nephropathy may be related to additional risk factors

To the Editor,

We read with interest the article entitled "Impact of continuation of metformin prior to elective coronary angiography on acute contrast nephropathy in patients with normal or mildly impaired renal functions" by Oktay et al. (1) published in the Anatolian Journal of Cardiology. The authors investigated the association of metformin treatment with contrast-induced acute kidney injury/contrast-induced nephropathy (CI-AKI/CIN). In this study, they concluded that periprocedural metformin treatment in patients with type 2 diabetes mellitus undergoing elective coronary angiography (CAG) with normal or mildly impaired renal functions (eGFR >60 mL/min/1.73 m²) was reliable with respect to the development of CI-AKI/CIN and lactic acidosis.

The exact pathophysiological mechanism underlying CI-AKI/CIN is still a matter of debate. However, it probably involves the direct toxic effect of contrast exposure (probably caused by high contrast media volume) and decreased renal medullary blood flow (particularly caused by heart failure, hypovolemia, hemodynamic instability, or anemia) that may contribute to the subsequent development of medullary ischemia and oxidative stress (2). In addition, a number of additional potential risk factors other than metformin use may also be attributed to CI-AKI/CIN development, an issue not discussed in the paper. It is of clinical importance to determine the contributions of hyperuricemia, hypoalbuminemia, and microalbuminuria to the development of CI-AKI/CIN.

In recent years, studies on the relationship between hyperuricemia and CI-AKI/CIN gradually appeared. In a meta-analysis of 18 relevant studies involving a total of 13,084 patients, subjects with hyperuricemia had a significantly increased risk of CI-AKI/CIN regardless of whether the effect size was adjusted or not. In this report, hyperuricemia in the subjects undergoing CAG and/or percutaneous coronary intervention resulted in significantly greater in-hospital mortality and incidence of CI-AKI/CIN requiring renal replacement therapy (3). Kumar et al. (4) reported that prophylactic oral administration of allopurinol (300 mg/day) was better than N-acetylcysteine (600 mg bd) alone or with saline hydration in the prevention of CI-AKI/CIN.

Hypoalbuminemia and microalbuminuria were also proven to be independent predictors of CI-AKI/CIN in patients with T2DM. In a study by Yang et al. (2), the incidence of CI-AKI/CIN in the positive urine albumin group was reported to be significantly higher than that in the trace and negative groups (positive vs. trace vs. negative: 18.5% vs. 6.7% vs. 3.9%, $p < 0.001$).

To better elucidate the effect of metformin treatment on CI-AKI/CIN development in patients undergoing coronary procedures with normal or mildly impaired renal functions, the

abovementioned confounding factors should have also been considered as they may contribute to the risk.

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Author's Reply

To the Editor,

We would like to thank the readers for their valuable comments related to our article entitled "Impact of continuation of metformin prior to elective coronary angiography on acute contrast nephropathy in patients with normal or mildly impaired renal functions" published in *Anatol J Cardiol* 2017; 18: 334-9 (1). Contrast-induced nephropathy (CIN) is associated with longer hospital stay and increased morbidity and mortality (2). Although the exact pathophysiology of CIN is not well-defined, several mechanisms such as renal medullary hypoxia, direct toxicity of contrast media, cytokine-induced oxidative stress, and inflammation have been proposed (3). As the readers have mentioned, multiple patient-related risk factors such as hyperuricemia, hypoalbuminemia, and microalbuminuria may contribute to the development of acute CIN after coronary angiography (CAG) (4, 5).

In our study, our main purpose was to evaluate the association between metformin continuation during CAG and CIN in patients with normal or mildly impaired renal functions. There-