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Microalbuminuria in patients with preserved renal function as a risk factor for contrast-Induced acute kidney injury following invasive coronary angiography

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ABSTRACT

Objectives: To investigate the association between pre-existing microalbuminuria among patients with preserved renal function and contrast- induced acute kidney injury (AKI) following coronary angiography.
Material and methods: 612 consecutive patients with preserved renal function (eGFR ≥ 60 ml/min and without macroalbuminuria) undergoing scheduled coronary angiography were stratified into microalbuminuria group (107 patients) and normal-albuminuria group (505 patients) according to the urine albumin to creatinine ratio (ACR) levels. Microalbuminuria was defined as ACR in the range of 30–300 mg/g and normal-albuminuria was defined as ACR <30 mg/g. Contrast-induced AKI was defined as a relative increase in serum creatinine (SCr) concentration of at least 25% or an absolute increase in SCr of 44.2 μmol/L within 72 h after the procedure.
Results: The peak increases of SCr in microalbuminuria group were larger than those in normal-albuminuria group (10.6 ± 12.4 μmol/L vs. 4.8 ± 8.9 μmol/L, P < 0.001). The incidence of AKI was higher in patients with microalbuminuria than those with normal-albuminuria (12.1% vs. 5.0%, P = 0.005). Multivariate analysis revealed that there was an association between microalbuminuria and contrast-induced AKI risk after adjusting for confounders.
Conclusion: Pre-existing microalbuminuria is associated with greater risk for AKI in patients with a preserved renal function who undergo scheduled coronary angiography.

1. Introduction

Contrast media is widely used in diagnostic imaging and catheter-based interventions [1]. Contrast-induced acute kidney injury (AKI) is regarded as one of the most clinically important complications after intravascular administration of iodinated CM. Contrast-induced AKI is the third leading cause of hospital-acquired acute renal failure. When there are no risk factors, the incidence of contrast-induced AKI is less than 5%. However, the incidence of contrast-induced AKI ranges from 11% to 50% in patients determined to be at high risk after standard assessment of risk factors [2]. Contrast media can cause acute renal insufficiency [3]. Furthermore, deterioration of renal function within 72 h after contrast media exposure is implicated as a poor prognosis in patients with pre-existing renal insufficiency. The occurrence of contrast-induced AKI has significant short- and long-term implications for patients' outcome [4]. Therefore, a high priority should be given to prevent this disorder. The definition of high-risk subgroups helps to focus on especially vulnerable patients and to implement intensive prevention strategies in these patients.

Currently, reduced eGFR is considered as the most important risk factor for contrast-induced AKI [5]. However, microalbuminuria is also an important marker for kidney injury. The importance of microalbuminuria for chronic kidney disease diagnosis has been described in the KDOQI guidelines [6]. Unfortunately, previous studies failed to pay enough attention to the effect of microalbuminuria on the incidence of contrast-induced AKI.

Proposed pathophysiologic mechanisms of contrast-induced AKI may be associated with endothelial dysfunction, resultant renal medullary hypoxia, and renal tubular damage [7]. Endothelial dysfunction and renal tubular damage may also be activated in the setting of microalbuminuria, which is common in patients with

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diabetes mellitus, hypertension, and some glomerular diseases [8]. However, it is unknown whether a combination of preexisted microalbuminuria and contrast media exposure increased the risk for contrast-induced AKI.

Microalbuminuria is defined as persistent elevation of albumin in the urine, of 30–300 mg/day. Use of the urine albumin to urine creatinine ratio (ACR) is recommended as the preferred screening strategy for detecting microalbuminuria [9]. Creatinine is used to correlate for the concentration of the urine. Prospective and epidemiologic studies have found that microalbuminuria is predictive, independently of traditional risk factors, of all-cause and cardiovascular mortality within groups of patients with diabetes or hypertension, and in the general population [10]. Since microalbuminuria is highly prevalent in hypertensive and diabetic populations [11], establishing whether pre-existing microalbuminuria is related to subsequent contrast-induced AKI risk would have important clinical implications.

Although reduced eGFR is a well-recognized risk factor for contrast-induced AKI, the incidence of contrast-induced AKI in patients with microalbuminuria has not been reported. Accordingly, we specifically sought to determine the relationship between pre-existing microalbuminuria and the risk for subsequent contrast-induced AKI after coronary angiography among patients with a preserved renal function.

2. Material and methods

2.1. Patients

We measured serum creatinine (SCr) and microalbuminuria levels before invasive coronary angiography (CAG) during hospitalization in patients undergoing scheduled CAG. Patients with eGFR $\geq$ 60 ml/min and without macroalbuminuria (defined as ACR >300 mg/g) were included in this study. Exclusion criteria were pregnancy, lactation, having been received contrast media within 7 days, emergent coronary angiography, eGFR <60 ml/min, macroalbuminuria, cardiogenic shock, pulmonary edema, multiple myeloma, mechanical ventilation, parenteral use of diuretics, use of *N*-acetylcysteine, and use of metformin or nonsteroidal anti-inflammatory drugs within 48 h of the procedure. Clinical characteristics of the included patients such as age, gender, body weight, blood glucose, blood pressure, baseline ACR, baseline serum creatinine (SCr), baseline eGFR, combined diseases, and concomitant medications were recorded. No contrast-induced AKI prophylaxis measures were used because the included patients were usually considered as the low risk population for contrast-induced AKI.

2.2. Procedures and outcomes

The cardiac catheterization procedures and interventions were performed according to practice standards for our center using the radial or femoral approach. Iohexol (Omnipaque, GE Healthcare Europe, 350 mg iodine/ml), a kind of most representative lower-osmolar non-ionic CM, was used in this study. CM was administered by intraarterial injection as necessary for each patient, and the total CM volume administered was recorded. The outcome for this study was the occurrence of contrast-induced AKI. Baseline SCr and microalbuminuria levels were measured during hospitalization that occurred before and closest to the time of coronary angiography. SCr levels were measured again at 24–48 h postdose and repeated at 48–72 h postdose. The highest SCr at 24–48 h or 48–72 h postdose was used to calculate the peak increases in SCr (the maximum value afterwards minus the value before). Contrast-induced AKI was defined as a relative increase in SCr concentration of at least 25% or an absolute increase in SCr of 44.2 μmol/L within 72 h after the procedure in the absence of other etiologies [2]. Microalbuminuria was defined as ACR in the range of 30–300 mg/g and normal-albuminuria was defined as ACR <30 mg/g. The Modification of Diet in Renal Disease formula was used to calculate eGFR [12]. All SCr and microalbuminuria levels were determined by laboratory personnel who measured it by autoanalyzer in the Department of Laboratory Medicine in the First Affiliated Hospital of Nanjing Medical University. If a patient underwent more than 1 coronary angiography procedure, the first procedure was considered for this analysis. All procedures were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000. The local ethical committee on human research approved the study protocol and informed consent was obtained from all patients.

2.3. Statistical analysis

In this study, continuous variables were summarized as mean ± standard deviation, and categorical data were presented as frequencies. Baseline characteristics were compared between groups using chi-square analysis for categorical variables andt test for continuous variables. SCr and eGFR were also compared between groups before contrast media administration. The primary analysis was to compare the incidence of contrast-induced AKI in patients with microalbuminuria to those with normal-albuminuria. The incidence of contrast-induced AKI was analyzed using Fisher exact test, two-sided. The difference in peak increases in SCr was analyzed using analysis of covariance, with predose measurement as covariate. Multivariate regression models were subsequently developed to evaluate whether the association between pre-existing microalbuminuria and contrast-induced AKI persisted after adjustment for other patient characteristics and potential confounders. Baseline variables with a $P < 0.05$ on univariate testing were simultaneously entered into the multivariate model. A value of $P < 0.05$ was considered significant. The statistical analysis was performed using SPSS software version 11.0 (SPSS Inc., Chicago, Illinois).

3. Results

3.1. Study patients

A total of consecutive 886 patients undergoing scheduled CAG were enrolled in the study. Of the 886 patients, 274 patients were excluded for variety of reasons (179 patients with eGFR <60 ml/min, 55 patients with macroalbuminuria, 32 patients with both eGFR <60 ml/min and macroalbuminuria, 3 patients with cardiogenic shock, 5 patients with acute myocardial infarction or cardiac related death during hospitalization). 612 patients with eGFR $\geq$ 60 ml/min and without macroalbuminuria were included in this study. Patients were stratified into microalbuminuria group (defined as ACR in the range of 30–300 mg/g, 107 patients) and normal-albuminuria group (defined as ACR <30 mg/g, 505 patients).

3.2. Baseline and procedural characteristics

Clinical characteristics were compared between patients with microalbuminuria and with normal-albuminuria and presented in Table 1. Gender, body weight, and diastolic pressure were not different between the two groups. Moreover, the prevalence of hypertension, dyslipidemia and chronic heart failure were also not different. Compared with patients with normal-albuminuria,