Incidence of Contrast-induced Nephropathy in Kidney Transplant Recipients

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ABSTRACT

Contrast-induced nephropathy (CIN) is responsible for one-third of acute kidney injuries (AKI) in the hospital setting. The incidence of CIN varies from 3% to 30%, depending on the preexisting risk factors, with higher incidence noted with diabetes mellitus, chronic kidney disease, and older age. Though CIN risk factors are common in kidney transplant recipients (KTRs), data about incidence of CIN in this population are sparse.

Methods. We retrospectively analyzed 124 consecutive patients transplanted at our center between January 2002 and December 2013 and received iodinated intravascular contrast with stable kidney function prior to contrast administration. CIN was defined as either an absolute rise in serum creatinine of $\geq$0.5 mg/dL or a $\geq$25% drop in estimated glomerular filtration rate (eGFR) after contrast administration.

Results. Seven of 124 (5.64%) patients developed CIN. Kidney function returned to baseline in 5 of the 7 patients within 3 weeks. In 2 patients serum creatinine remained elevated due to recurrent AKI episodes from other causes. Dialysis was not required in any patient. Calcineurin inhibitors (CNIs) were being used in 95% patients at the time of contrast administration. Diabetes mellitus, baseline serum creatinine, age, race, gender, and the use of ACE inhibitor, angiotensin receptor blocker, diuretic, or prophylaxis with intravenous hydration $\pm$ *N*-acetylcysteine did not affect the incidence of CIN.

Conclusion. Incidence of CIN in KTRs was low in our study (5.6%), much less than previously reported. This low incidence may be related to the high baseline eGFR (>70 mL/min/1.73 m^2) and use of hypo-osmolar contrast in our patients. In KTRs with baseline eGFR >70 mL/min, the incidence of CIN is low despite the concurrent use of nephrotoxic CNI.

CONTRAST-INDUCED NEPHROPATHY (CIN) is characterized by the development of acute kidney injury (AKI) after the administration of intravascular iodinated radiocontrast (hereafter referred to as contrast) in the absence of any other etiology of AKI [1]. Incidence of CIN for those without preexisting renal impairment ranges from 0.6% to 2.3%; however, risk increases to 12% to 26%, or even higher for those with renal disease or diabetes mellitus (DM) [2,3]. Despite frequent and favorable recovery of kidney function after CIN, morbidity and mortality are high in patients who experience CIN.

In a recent study, CIN was associated with poor short- and long-term outcomes [4]. In this study of nearly 3000 patients who underwent percutaneous coronary intervention (PCI), 16% developed AKI and subsequently experienced significantly higher risk of cardiovascular events compared with those without AKI. In addition, those with AKI had higher mortality rates at 30 days and 3 years (8.0% vs 0.9% and 16.2% vs 4.5%, respectively). On multivariate analysis, CIN was associated with a 53% increased risk of net adverse clinical events, a 56% increased risk of major adverse cardiac events, and an 80% increased risk of death at 3 years.

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The well-known risk factors for the development of CIN include preexisting renal impairment, DM, advanced age, periprocedural intravascular volume depletion, congestive heart failure, volume and type of contrast administered, and concomitant use of other nephrotoxic drugs [1].

Kidney transplant recipients (KTRs) may be at higher risk of CIN due to high prevalence of chronic kidney disease, DM, and cardiovascular disease and the concurrent use of a nephrotoxic calcineurin inhibitor (CNI) for immunosuppression (a CNI [cyclosporine or tacrolimus] is used in more than 95% of KTRs). Presence of underlying chronic kidney disease has been recognized as the most important risk factor for the development of CIN [1]. Due to early immune and nonimmune injury, most allografts end up with reduced glomerular filtration rate (GFR). The average GFR in KTRs is between 50 and 70 mL/min/1.73 m^2 [5]. This, along with the near universal use of a nephrotoxic CNI, may place KTRs at higher risk for CIN.

Scant information is available about incidence of CIN in KTRs. To our knowledge, only 4 studies (all retrospective) exist and were published in 1975, 1983, and 2000 [6–9]. Only 1 of these studies was done after the introduction of CNIs [6]. There are no prospective studies of CIN in KTRs.

The objective of our study was to assess incidence of CIN in a large group of KTRs on currently used immunosuppressive regimens. We also wanted to evaluate the effect of CNI use and other previously known risk factors on the incidence of CIN in KTRs.

METHODS

We retrospectively identified from our institutional database 124 consecutive KTRs (transplanted between 2002 and 2013) who received intravascular contrast and had stable kidney function before contrast administration. Patients received contrast either for CT scan (77%), pulmonary angiogram (18%), or cardiac catheterization (4.8%).

We collected the following demographic data from patients: race, age, gender, date and type of contrast study, date and type of transplantation, type and volume of contrast used, and any prophylaxis used to prevent CIN. Protocol immunosuppression was comprised of triple therapy (tacrolimus, mycophenolate mofetil, and steroids) in most patients. A CNI was being used in 118 (95%) patients at the time of contrast administration. For inclusion in the study, a patient's kidney transplant function had to be stable (defined as <15% day-to-day variation in baseline serum creatinine level prior to contrast administration) to ensure that causes of AKI other than CIN were not already causing renal injury. Only patients in whom pre- and post-contrast (at 24–48 hours, 72 hours, and 3 weeks) serum creatinine levels were available were included in the study.

All patients received hypo-osmolal contrast. CIN was defined (consistent with prior literature) [1] as an absolute rise in serum creatinine of ≥0.5 mg/dL or a ≥25% decrease in eGFR (calculated using the MDRD-4 formula), from baseline value at 48 to 72 hours following the exposure to contrast. Diagnosis of CIN was made on clinical grounds after excluding other causes of AKI.

The primary endpoint was the incidence of CIN. Secondary endpoints were to assess the association of CIN and the following: age; race; gender; DM; hypertension; baseline serum creatinine level or eGFR; baseline serum bicarbonate; use of ACE inhibitor (ACE-i), angiotensin receptor blocker (ARB), diuretic, or prophylaxis (IV volume expansion ± *N*-acetylcysteine); and volume of contrast administered. Our IRB approved this study.

Table 1. Baseline Characteristics

Variable	CIN n = 7	Non-CIN n = 117	*P* Value
Age (y), mean ± SD	46.57 ± 16.51	51.87 ± 12.47	.4336
Race, n (%)			
White	2 (29%)	61 (52%)	.3337
African American	4 (57%)	48 (41%)	
Other	1 (14%)	9 (7%)	
Females, n (%)	2 (29%)	34 (29%)	.6837
DM, n (%)	4 (57%)	69 (58%)	1.0000
Hypertension, n (%)	7 (100%)	107 (91%)	1.0000
CIN use, n (%)	7 (100%)	111 (94%)	1.0000
Mycophenolate mofetil use, n (%)	7 (100%)	102 (86%)	.5933
mTOR-inhibitor use, n (%)	0 (0%)	9 (8%)	1.0000
ACE-inhibitor or ARB use, n (%)	2 (29%)	26 (22%)	.6552
Diuretic use, n (%)	1 (14%)	20 (17%)	1.000
Serum creatinine (mg/dL), mean ± SD	1.03 ± 0.09	1.14 ± 0.33	.3677
eGFR (mL/min/1.73 m^2), mean ± SD	78.25 ± 11.41	74.11 ± 30.58	.7224
Serum bicarbonate (mg/dL), mean ± SD	25.08 ± 3.38	24.02 ± 3.33	.4838
Volume of contrast (mL), mean ± SD	108.5 ± 24.16	125 ± 15.81	.0508
Volume expansion, (%)	82 (70%)	5 (71%)	1.000
NAC given, n (%)	3 (43%)	35 (30%)	.4706

Abbreviations: CIN, contrast-induced nephropathy; SD, standard deviation; ARB, angiotensin receptor blocker; ACEi, angiotensin-converting enzyme inhibitor; NAC, *N*-acetylcysteine; CNI, calcineurin inhibitor.

Statistics

Statistical analysis was performed using SAS software version 9.3 (SAS Institute, Inc., Cary, N.C., United States). Categorical variables are presented as frequencies and percentages. Continuous variables are presented as mean ± standard deviation. Student *t* test was used for group comparisons for continuous data with normal distribution. Categorical data comparisons were performed using the χ^2 test or the Fisher exact test.

RESULTS

CIN developed in 7/124 patients (5.64%). The baseline characteristics of patients and risk factors for CIN stratified by the presence or absence of CIN are shown in Table 1. Because of the low overall event rate, the study was not adequately powered to examine the discriminatory power of individual variables as predictors of contrast nephropathy. Nevertheless, there was no significant association between CIN and any of the following: age, race, gender, DM, hypertension, baseline serum creatinine level or eGFR, use of ACEi or ARB, diuretic, prophylaxis (IV volume expansion ± *N*-acetylcysteine),