LETTER TO THE EDITORS

The fear for contrast-induced nephropathy in kidney transplant recipients: time for a paradigm shift?

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Dear Editors,

A recently published article in the Lancet (AMACING trial) challenges a long-standing clinical consensus: intravenous (i.v.) volume expansion with isotonic saline as a prophylactic measure for iodinated contrast-induced nephropathy (CIN) [1]. The randomized trial showed that—in patients with an estimated glomerular filtration rate (eGFR) of 30–59 mL/min/1.73 m^2, undergoing an elective procedure—as compared to i.v. hydration, no prophylaxis is noninferior in preventing CIN.

While caring for kidney transplant recipients (KTRs), we are often challenged by the widely applied clinical practice of using iodinated contrast for diagnostic and interventional purposes, such as computed tomography (CT), CT angiography, and endovascular procedures. On paper, the current reluctance to avoid iodinated contrast after transplantation may delay diagnosis of post-transplant complications. This could possibly be avoided, as the median (2.5–97.5 percentile) measured GFR (mGFR) at 10 weeks post-transplant is 51 (29–78), indicating that most KTR have a mGFR comparable to the patients enrolled in the AMACING trial [2]. Previous retrospective cohort studies have reported on the incidence of CIN in KTRs, showing an incidence of 2.9–13.3% after infusion of iodinated contrast for CT, 12.9% after cardiac catheterization, 8.1% after renal

Table 1. Literature overview on the incidence of contrast-induced nephropathy in kidney transplant recipients.

	Abu Jawdeh (2017) [3]	Fananapazir (2016) [4]	Bostock (2016) [5]	Fananapazir (2016) [6]	Haider (2015) [7]
Sample size	76	104	40	37	124
Inclusion period	2000–2014	2005–2015	2003–2014	2006–2014	2002–2013
Intervention	CT (59%); Cardiac cath (41%)	CT	Endovascular aortic aneurysm repair	Renal graft catheter arteriography	CT (77%); Cardiac cath (5%); pulmonary angiogram (18%)
Prophylaxis					
IV volume expansion	53%	85%	Not mentioned	58%	70%
N-acetylcysteine	36%	14%		15%	30%
Definition of CIN	Increase in sCr of ≥0.3 or ≥25% drop in eGFR	Increase in sCr of (i) ≥0.3 or (ii) 0.5	Increase in sCr of ≥0.5	Increase in sCr of ≥0.5	Increase in sCr of ≥0.5 or ≥25% drop in eGFR
Incidence of CIN	CT: 6 (13.3%) Cath: 4 (12.9%)	(i) 7 (6.7%) or (ii) 3 (2.9%)	5 (12.5%)	3 (8.1%)	7 (5.6%)
Resulting in dialysis	None	None	1 (2.5%)	None	None

Cardiac cath, cardiac catheterization; CT, computed tomography; sCr, serum creatinine in mg/dL.

doi:10.1111/tri.13277

graft catheter arteriography, and 12.5% after endovascular aortic aneurysm repair (Table 1) [3–7]. This, compared to the most recent meta-analysis on CIN in the general population, reporting a 7.2% incidence of CIN after iodinated contrast CT [8]. Even though the studies with KTRs are small and retrospective, based on these data, the *Contrast Medium Safety Committee* of the *European Society of Urogenital Radiology*, concluded that there is insufficient evidence to substantiate a higher incidence of CIN in KTRs than in the nontransplant population [9]. Hereby, KTRs should be treated in concordance with nontransplant recipients with a similar eGFR. As such, the paradigm shift on prophylaxis for CIN in the general population, supported by the AMACING trial, could also be applied to KTRs: for patients with an eGFR above 59, the risk for CIN is low, and prophylaxis is not required. Moreover, for patients with an eGFR between 30 and 59, no prophylaxis can be considered as a safe alternative for elective procedures using iodinated contrast. Meanwhile, for patients with an eGFR under 30, prophylaxis with i.v. sodium chloride or i.v. sodium bicarbonate is advised. However, these patients are underrepresented in the literature.

Based on the current literature, a clear recommendation for either i.v. sodium chloride or i.v. sodium bicarbonate cannot be stated. The results of the PRESERVE trial, performed in patients with an eGFR of 15–44.9 or 45–59.9 in diabetic patients, were presented in a recent NEJM article. When comparing patients receiving either i.v. sodium bicarbonate or i.v. sodium chloride, there was no significant difference in the incidence of CIN after angiography, indicating that both types of prophylaxis lead to similar outcomes [10].

In short, there has been a paradigm shift on prophylaxis for CIN in the general population: going from prophylaxis in patients with an eGFR under 60 to prophylaxis for only those high-risk patients with an eGFR under 30. This beckons the discussion to equate KTRs to nontransplant patients in contrast to administration procedures, with the suggestion to make an eGFR based decision on the need for prophylaxis for each specific KTR. Implementation of these recommendations will arguably result in faster and more accurate diagnosis of post-transplant complications, as contrast-enhanced diagnostic and intervention procedures are, in many cases, the standard of care.

REFERENCES

1. Nijssen EC, Rennenberg RJ, Nelemans PJ, *et al.* Prophylactic hydration to protect renal function from intravascular iodinated contrast material in patients at high risk of contrast-induced nephropathy (AMACING): a prospective, randomised, phase 3, controlled, open-label, non-inferiority trial. *Lancet* 2017; **389**: 1312.
2. Salvador CL, Hartmann A, Åsberg A, Bergan S, Rowe AD, Mørkrid L. Estimating glomerular filtration rate in kidney transplant recipients: comparing a novel equation with commonly used equations in this population. *Transplant Direct* 2017; **3**: e332.
3. Abu Jawdeh BG, Leonard AC, Sharma Y, *et al.* Contrast-induced nephropathy in renal transplant recipients: a single center experience. *Front Med* 2017; **4**: 64.
4. Fananapazir G, Troppmann C, Corwin MT, Nikpour AM, Naderi S, Lamba R. Incidences of acute kidney injury, dialysis, and graft loss following intravenous administration of low-osmolality iodinated contrast in patients with kidney transplants. *Abdom Radiol* 2016; **41**: 2182.
5. Bostock IC, Zarkowsky DS, Hicks CW, *et al.* Outcomes of endovascular aortic aneurysm repair in kidney transplant recipients: results from a national quality initiative. *Am J Transplant* 2016; **16**: 2395.
6. Fananapazir G, Troppmann C, Corwin MT, Bent CK, Vu CT, Lamba R. Incidence of contrast-induced nephropathy after renal graft catheter arteriography using iodine-based contrast medium. *Am J Roentgenol* 2016; **206**: 783.
7. Haider M, Yessayan L, Venkat KK, Goggins M, Patel A, Karthikeyan V. Incidence of contrast-induced nephropathy in kidney transplant recipients. *Transplant Proc* 2015; **47**: 379.
8. Aycock RD, Westafer LM, Boxen JL, Majlesi N, Schoenfeld EM, Bannuru RR. Acute kidney injury after computed tomography: a meta-analysis. *Ann Emerg Med* 2018; **71**: 44.e4.
9. van der Molen AJ, Reimer P, Dekkers IA, *et al.* Post-contrast acute kidney injury – Part 1: definition, clinical features, incidence, role of contrast medium and risk factors. *Eur Radiol* 2018; doi: 10.1007/s00330-017-5246-5. [Epub ahead of print].
10. Weisbord SD, Gallagher M, Jneid H, *et al.* Outcomes after angiography with sodium bicarbonate and acetylcysteine. *N Engl J Med* 2018; **378**: 603.