

EDITORIAL COMMENT

# The Imperative of Reducing Contrast Dose in Percutaneous Coronary Intervention\*



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Contrast nephropathy is a major concern of interventional cardiologists caring for renally vulnerable patients. It can result in a spectrum of complications, ranging from prolonged hospitalization, to permanent degradation of renal function, to dialysis, and even to death. Furthermore, the threat of this iatrogenic problem often limits the use of beneficial radiographic diagnostic and therapeutic procedures for patients with atherosclerotic coronary artery disease who are at high risk for contrast nephropathy, resulting in suboptimal treatment of their ischemia.

Currently, prevention of contrast nephropathy is generally limited to optimizing pre-procedure renal function and ensuring adequate periprocedural patient hydration, either with intravenous normal saline or bicarbonate solution. Extensive investigative efforts at pharmacologic prevention using agents such as mannitol, furosemide, acetylcysteine, ascorbic acid, dopamine, fenoldopam, and statins have so far shown disappointing results, and consequently, none are recommended in the latest percutaneous coronary intervention (PCI) guidelines (1).

A promising preventative strategy, which has been underutilized, is the reduction of contrast dose. Of all the basic risk factors for contrast nephropathy, including chronic kidney disease, congestive heart failure, hypotension, anemia, age, diabetes mellitus, and contrast volume, contrast volume is the most substantially and practically

“modifiable” (2). Several previous studies have demonstrated a strong association between contrast dose and the occurrence of contrast nephropathy (Table 1). This evidence suggests that reducing contrast dose will greatly benefit vulnerable patients and supports the need for contrast-sparing PCI strategies (2-4).

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The MOZART (Minimizing cOntrast utiliZation With IVUS Guidance in coRonary angioplasTy) study, in this issue of *JACC: Cardiovascular Interventions*, is an important randomized controlled study demonstrating that the aggressive use of intravascular ultrasound (IVUS)-based strategy can dramatically reduce the contrast dose during PCI (5). In this study, 83 patients with IVUS-amenable severe coronary artery disease underwent PCI with standard contrast reduction techniques, with or without additional IVUS-based contrast reduction techniques. The standard contrast reduction techniques were similar to those described by Nayak et al. (6) and included the following: 1) meticulous pre-procedural planning based on diagnostic angiography; 2) the use of reference images, small-caliber catheters, small-volume syringes, diluted contrast, and high-resolution cine-angiography; and 3) the avoidance of catheters with side holes, “puff-testing,” and exceeding a contrast volume-to-creatinine clearance ratio of 2. IVUS-based contrast reduction techniques included aiming for a single baseline angiogram with either 1 or no completion angiogram, while using IVUS—without angiography—to do the following: 1) define lesion length and reference diameter; 2) determine lesion preparation techniques, including, whenever possible, the selection of a direct stenting strategy; 3) guide balloon and stent positioning using stored fluoroscopic images of the IVUS probe to “mark” the proximal and distal borders of the lesion; and 4) check results of

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pre-dilation and stenting and to guide post-dilation and additional stent placement. The use of standard contrast reduction techniques resulted in a low average contrast dose of 64 ml<sup>3</sup>/procedure (compared with a historical 148 ml<sup>3</sup>/procedure in similar patients at their center). The addition of IVUS-based contrast reduction techniques further reduced average dose by approximately two-thirds, to a very low 20 ml<sup>3</sup>/procedure, with a range of 3 ml<sup>3</sup> to 54 ml<sup>3</sup>, in 41 patients randomized to this strategy (p < 0.001).

The only clinical disadvantage of the IVUS-based contrast reduction techniques observed in this study was a longer procedure time (+14 min), which was likely due to IVUS image interpretation. There were no signals of potential safety concerns. One might also reasonably speculate that the cost of the IVUS-based strategy is higher because of the use of IVUS, although this would likely be at least partially offset by the reduced contrast use and complications. Furthermore, the IVUS-based strategy may well result in reduced target vessel-associated major adverse cardiovascular events, as suggested by a recent meta-analysis of IVUS-guided versus angiography-guided drug-eluting stenting (7).

A major limitation of this study is the selection of patients who were suitable for IVUS guidance (“all target vessels needed to be amenable to IVUS imaging at baseline [i.e., before any balloon dilatation], as judged by an experienced interventionalist”) (5). This potentially limits the findings of this study to patients whose coronary anatomy permits easy passage of the IVUS catheter, that is, those with proximal lesions in nontortuous, noncalcified arteries with relatively large minimal luminal areas. In fact, patients at high risk for contrast nephropathy (patients with long-standing hypertension, diabetes, and chronic renal insufficiency) tend to be less likely to have such suitable anatomy. Another limitation is the necessary lack of blinding of the potentially biased investigators/interventionalists to the strategy. Both of these limitations could result in an overestimation of the magnitude of contrast reduction that will be seen in everyday practice. A final limitation is that the study was not powered to detect clinical efficacy. In fact, although there was a trend toward reduced contrast nephropathy (19.0% vs. 7.3%), it was not statistically significant (p = 0.2). A larger prospective, randomized controlled trial showing the clinical efficacy of reducing contrast dose would be compelling and desirable. However, considering the strong intellectual rationale and abundant observational evidence supporting the benefit of contrast dose reduction,

**TABLE 1 Contrast Dose Associated With PCI-Related Nephropathy**

First Author, Year (Ref. #)	Study Population, n and Procedure	Contrast Dose Predictive of Increased Nephropathy Risk
Freeman et al., 2002 (14)	16,592 PCI	≥5 ml × body wgt/SCr
Laskey et al., 2007 (15)	3,179 PCI	≥3.7 contrast vol/eGFR ratio
Nyman et al., 2008 (16)	391 primary PCI	≥1 g iodine/eGFR
Marenzi et al., 2009 (3)	561 primary PCI	≥5 ml × body wgt/SCr
Brown et al., 2010 (17)	10,065 PCI	≥5 ml × body wgt/SCr
Mager et al., 2011 (18)	871 primary PCI	≥3.7 contrast vol/eGFR ratio
Gurm et al., 2011 (19)	58,957 PCI	≥2.0 contrast vol/eGFR ratio
Liu et al., 2011 (20)	277 primary PCI	≥2.4 contrast vol/eGFR ratio
Tan et al., 2013 (4)	1,135 PCI	≥2.6 contrast vol/eGFR ratio
Kooiman et al., 2014 (21)	82,120 PCI	≥3.0 contrast vol/eGFR ratio

eGFR = estimated glomerular filtration rate; PCI = percutaneous coronary intervention; SCr = serum creatinine; vol = volume; wgt = weight.

the lack of such a study should not prevent adoption of safe strategies that reduce contrast dose in high-risk patients. Therefore, all things considered, the IVUS-based contrast reduction techniques described in MOZART should be applicable to those patients at highest risk of contrast nephropathy now.

Perhaps the most important message of this trial is that drastic reductions in contrast dose can be achieved in many patients if deliberately and thoughtfully pursued. Strategies other than IVUS-guidance that may reduce contrast volume include the use of biplane angiography, rotational angiography, automated contrast injectors, and subselective coronary artery engagement (8-11). A “contrast conservation system” to restrict excess contrast reflux into the aorta for use during manual coronary injections has shown a 40% reduction in contrast dose and is under continued development (12). In addition, an innovative device designed to remove contrast from the coronary sinus has been developed (13).

Patients with atherosclerotic coronary artery disease and high susceptibility to contrast nephropathy are increasing rapidly in number, due in large part to the aging population and the concomitant increase in chronic kidney disease. To serve this important group and provide them the benefits of intravascular radiographic procedures such as PCI, it is imperative that we continue to creatively develop and systematically disseminate techniques that diminish contrast dose.

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