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# Intravascular Ultrasound Guidance to Minimize the Use of Iodine Contrast in Percutaneous Coronary Intervention

## The MOZART (Minimizing cOntrast utiliZation With IVUS Guidance in coRonary angioplasTy) Randomized Controlled Trial

José Mariani Jr, MD,* Cristiano Guedes, MD,* Paulo Soares, MD, PhD,* Silvio Zalc, MD, PhD,* Carlos M. Campos, MD,*† Augusto C. Lopes, MD,‡ André G. Spadaro, MD,* Marco A. Perin, MD, PhD,* Antonio Esteves Filho, MD,* Celso K. Takimura, MD, PhD,* Expedito Ribeiro, MD, PhD,* Roberto Kalil-Filho, MD, PhD,* Elazer R. Edelman, MD, PhD,‡§ Patrick W. Serruys, MD, PhD,†‖ Pedro A. Lemos, MD, PhD*

## ABSTRACT

**OBJECTIVES** The aim of this study was to evaluate the impact of intravascular ultrasound (IVUS) guidance on the final volume of contrast agent used in patients undergoing percutaneous coronary intervention (PCI).

**BACKGROUND** To date, few approaches have been described to reduce the final dose of contrast agent in PCIs. We hypothesized that IVUS might serve as an alternative imaging tool to angiography in many steps during PCI, thereby reducing the use of iodine contrast.

**METHODS** A total of 83 patients were randomized to angiography-guided PCI or IVUS-guided PCI; both groups were treated according to a pre-defined meticulous procedural strategy. The primary endpoint was the total volume contrast agent used during PCI. Patients were followed clinically for an average of 4 months.

**RESULTS** The median total volume of contrast was 64.5 ml (interquartile range [IQR]: 42.8 to 97.0 ml; minimum, 19 ml; maximum, 170 ml) in the angiography-guided group versus 20.0 ml (IQR: 12.5 to 30.0 ml; minimum, 3 ml; maximum, 54 ml) in the IVUS-guided group ($p < 0.001$). Similarly, the median volume of contrast/creatinine clearance ratio was significantly lower among patients treated with IVUS-guided PCI (1.0 [IQR: 0.6 to 1.9] vs. 0.4 [IQR: 0.2 to 0.6, respectively; $p < 0.001$). In-hospital and 4-month outcomes were not different between patients randomized to angiography-guided and IVUS-guided PCI.

**CONCLUSIONS** Thoughtful and extensive use of IVUS as the primary imaging tool to guide PCI is safe and markedly reduces the volume of iodine contrast compared with angiography-alone guidance. The use of IVUS should be considered for patients at high risk of contrast-induced acute kidney injury or volume overload undergoing coronary angioplasty. (Minimizing cOntrast utiliZation With IVUS Guidance in coRonary angioplasTy [MOZART]; NCT01947335) (J Am Coll Cardiol Intv 2014;7:1287–93) © 2014 by the American College of Cardiology Foundation.

From the *Department of Interventional Cardiology, Heart Institute (InCor), University of São Paulo Medical School, Sao Paulo, Brazil; †Thoraxcenter, Erasmus Medical Center, Rotterdam, the Netherlands; ‡Institute of Medical Engineering and Science, Massachusetts Institute of Technology, Cambridge, Massachusetts; §Cardiovascular Division, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; and the ‖Imperial College London, London, United Kingdom. The present study is an investigator-sponsored study partially supported by Boston Scientific Corporation. Dr. Lemos is supported in part by a grant from the National Council for Scientific and Technological Development (CNPq)–Brazil. Dr. Edelman is supported in part by a grant from the U.S. National Institutes of Health (R01 GM49039). Dr. Lopes is supported by an Arie Fellowship from the Brazilian Society of Interventional Cardiology. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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**ABBREVIATIONS AND ACRONYMS**

**CI-AKI** = contrast-induced acute kidney injury

**IVUS** = intravascular ultrasound

**IQR** = interquartile range

**PCI** = percutaneous coronary intervention

Contrast-induced acute kidney injury (CI-AKI) is a potential complication of diagnostic and therapeutic angiographic procedures. Almost unanimously, previous studies have shown that CI-AKI is associated with worse clinical outcomes (1). It remains debatable, however, whether CI-AKI is solely a marker for future morbimortality or, conversely, it is also causally implicated in the occurrence of adverse events (1,2).

A number of strategies have been tested to reduce the incidence of CI-AKI. Vigorous fluid administration before and after the procedure is considered the most important prophylactic scheme for patients at risk of CI-AKI (3,4). Multiple other preventive measures have been evaluated in clinical studies, but none has been widely adopted, and, in practice, CI-AKI persists as a major clinical problem for patients undergoing angiographic procedures (4–13).

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Although the incidence of CI-AKI is modulated by several clinical characteristics, the volume of iodine contrast seems to be a major factor leading to CI-AKI, independently of the baseline risk profile (14–18). Curiously, thus far, few approaches have been described to reduce the primary cause of CI-AKI after PCI, namely, the contrast agent dose (19–22). It is of note that, in addition to be of potential benefit for patients at risk of CI-AKI, strategies to decrease the use of contrast may also be valuable for other subgroups of patients, such as those at risk of volume overload.

Intravascular ultrasound (IVUS) is largely used to guide percutaneous coronary interventions (PCIs) (23). Because of its ability to accurately measure lumen, plaque, and vessel dimensions, it is possible that IVUS might serve as an alternative tool to angiography in many steps during PCI. We therefore hypothesized that IVUS imaging during coronary angioplasty may lead to a reduced use of contrast media. The present report describes the primary endpoint analysis of the MOZART (Minimizing cOntrast utiliZation With IVUS Guidance in coRonary angioplasTy) randomized controlled trial study, which evaluated the impact of thorough IVUS guidance on the final dose of contrast agent used in patients undergoing PCI.

**TABLE 1 Guidelines to Reduce the Volume of Contrast During Percutaneous Coronary Angioplasty (To Be Applied in Both Study Arms)**

| |
|---|
| Awareness of the baseline creatinine clearance to ensure that contrast use does not to exceed a volume-to-creatinine clearance ratio of 2. All actions should be taken to never exceed a ratio of 3, whenever possible. |
| Detailed analysis of the diagnostic coronary angiography to plan the interventional procedure (e.g., choice for best projections, selection of treatment strategies) and anticipate potential complications. |
| If the diagnostic coronary angiography was performed recently and of good quality, consider avoiding any baseline angiography during percutaneous coronary intervention. In this case, the diagnostic angiography, displayed on an auxiliary video monitor, should be used as a baseline reference. |
| Extensive use of auxiliary video monitors with reference images of the target vessel anatomy during the procedure. |
| Extensive use of online x-ray (noncontrast) stent enhancement post-processing techniques. |
| Small-diameter guiding catheters (5- or 6-F) with no side holes. |
| Small-volume syringes for contrast injection (3 or 5 ml). |
| Extensive use of diluted contrast during the procedure (at least 1:1). |
| All contrast injections must be done during acquisition (not fluoroscopy) for better visualization of target segments and to allow for repeat video loops. |
| Avoid unnecessary "puff testing" of contrast. |
| Liberal use of high acquisition rates. Increased acquisition rates (i.e., >15 frames per second) may be used during the procedure to improve angiographic image quality, particularly in patients with high heart rate or for fast-moving target segments (e.g., midright coronary artery or midleft circumflex artery). |
| Before insertion of any new interventional material into the guiding catheter (e.g., balloons, stents), caution must be taken to make sure that the lumen of the catheter is free of contrast. |

## METHODS

**PATIENT POPULATION.** Patients 18 years of age or older scheduled for PCI were considered for enrollment in the MOZART trial. Included patients were at high risk of CI-AKI or volume overload, according to the presence of ≥1 of the following criteria: 1) older than >75 years of age; 2) diabetes; 3) acute ischemic syndrome needing urgent or emergent PCI; 4) creatinine clearance <60 ml/min/1.73 $m^2$ or a single remaining kidney or previous renal transplantation; 5) congestive heart failure, pulmonary congestion, severe left ventricular dysfunction (ejection fraction <45%), cardiogenic shock, or intra-aortic balloon pumping. Angiographic eligibility required that all target vessels be amenable to IVUS imaging at baseline (i.e., before any balloon dilation), as judged by an experienced interventionalist. Exclusion criteria included use of iodinated contrast agents <72 h or other nephrotoxic agents <7 days before procedure, known allergy to contrast agents, and unstable or unknown renal function before PCI. The study was approved by the institutional review board, and signed written informed consent was obtained from every patient.

**STUDY DESIGN, TREATMENT PROTOCOL, AND FOLLOW-UP.** All patients at high risk of CI-AKI received intravenous hydration for 12 h pre- and 12 h post-PCI. The interventional plan was left to the discretion of the operator, but regardless of the allocated arm, operators were strongly recommended to follow strict strategies to reduce the total volume of contrast for all patients, as summarized in Table 1.

Saline (NaCl 0.9%) infusion was recommended at a dose of 1 ml/kg body weight per hour (24) and reduced to 0.5 ml/kg/h for those at high risk of volume overload (e.g., reduced left ventricular function or overt heart failure) (15). The use of N-acetylcysteine or sodium bicarbonate was left to the operator's discretion. All percutaneous procedures were performed using nonionic, low-osmolar or iso-osmolar, iodine-based contrast media (iopromide [Ultravist, Bayer Pharma AG, Berlin, Germany] or iodixanol [Visipaque, GE Healthcare Ireland, Cork, Ireland]).

Patients were randomized nonblindedly in blocks via an electronic system in a 1:1 ratio to angiography-guided PCI or IVUS-guided PCI.

For those allocated to the IVUS-guided group, IVUS imaging was performed with the Atlantis SR Pro Imaging Catheter 40 MHz connected to an iLab Ultrasound Imaging System (both by Boston Scientific Corporation, Natick, Massachusetts). Vessels were imaged during automated pullback at 0.5 mm/s, but additional manual runs were strongly stimulated to allow for detailed analysis of specific issues. Operators were encouraged to use IVUS to the limit of its potential, aiming to ultimately replace angiographic imaging. **Table 2** provides a detailed description of the contrast-avoiding IVUS strategy. A final IVUS pullback was required to document the results at the end of the procedure, targeting achievement of complete stent apposition, without residual plaque burden at the stent edges (ideally <50% plaque burden) or major edge dissections and maximization of stent expansion (ideally the intrastent minimal luminal area should be >90% of the smallest reference lumen area).

After the index procedure, patients were followed for 30 days with the main objective of detecting safety clinical events, namely, death, myocardial infarction, or unplanned reinterventions.

**ENDPOINT DEFINITIONS AND STATISTICAL CONSIDERATIONS.** The primary endpoint of the MOZART trial was the total volume of contrast agent used during PCI. The present report also analyzes the in-hospital and post-discharge incidence of adverse clinical events, a predefined safety endpoint. All deaths were considered for analysis. Myocardial infarctions were classified as 1) spontaneous; 2) secondary to ischemic imbalance; 3) leading to death with biomarkers unavailable; 4) post-PCI; 5) post-coronary bypass surgery; or 6) related to stent thrombosis (25). Stent thrombosis was further classified according to the degree of certainty as definite, probable, or possible (26). Unplanned coronary reinterventions were computed if required by a stenosis located in any segment of the epicardial vessel treated at the index procedure.

**TABLE 2 Technical Description of IVUS Guidance to Minimize Contrast Use**

| |
|---|
| General rule: IVUS guidance aims to minimize contrast use. However, noncontrast radiographic imaging is not precluded. Fluoroscopy and cine runs without contrast might be used (and are encouraged), for instance, to visualize the stent limits and borders, identify the position of IVUS probe inside the vessel, and register balloon expansion. |
| Aim for a single angiographic acquisition at baseline. |
| Extra baseline views are almost always unnecessary when using IVUS. |
| Use IVUS, not angiography, as the main source of information to plan PCI strategy. |
| Baseline as well as interim IVUS imaging runs should be used liberally to evaluate intervening results and help plan the next steps. |
| Use baseline IVUS imaging to decide whether to use direct stenting. |
| For short, noncalcified, not severely obstructive lesions, consider direct stenting. |
| Conversely, long fibrocalcified, diffusely diseased segments should undergo lesion preparation, with balloon dilation or rotablation. |
| Use IVUS, not angiography, to check the results of pre-dilation. |
| The need for additional dilation and the occurrence of dissections are readily assessable by IVUS. |
| For stent sizing, aim to use IVUS imaging only, not angiography. |
| Identification of the proximal and distal reference segments is central to IVUS selection of stent diameter and length. |
| Liberal use of manual IVUS imaging to precisely identify the 2 proximal and distal reference spots. |
| Selection of stent diameter: |
| Stent diameter is primarily based on the size of reference segments. |
| IVUS guidance to select stent diameter is particularly informative in lesions with a large disproportion between the reference segment sizes, in diffusely diseased arteries, or lesions with extreme remodeling patterns (either positive or negative). |
| Selection of stent length: |
| Stent length should aim to cover from normal to normal segments ideally. |
| Stent length should be selected based on the longitudinal measurements of an IVUS imaging run acquired with automatic pullback at known speed (preferably 0.5 mm/s). |
| Also, manual IVUS imaging can be used as an auxiliary practical way of assessing/confirming stent length. With the IVUS probe turned on in continuous imaging, the proximal and distal reference points are iteratively selected. The distance between the chosen landing zones can be easily measured manually using the length measurement registered in the electronic display of the pullback device. |
| Minimize contrast using IVUS for stent positioning. |
| Obtain an x-ray (without contrast) with the IVUS probe at the proximal and distal references spots. |
| Store these images and display them in an auxiliary monitor during stent placement to guide positioning, minimizing contrast "puffing." |
| Use IVUS, not angiography, to verify the results of stent implantation. |
| Most often, stent underexpansion is better managed with higher pressure post-dilation with an appropriately sized noncompliant balloon. |
| Incomplete apposition should be treated with post-dilation using appropriately sized semicompliant balloons. |
| Use IVUS to judge the need for additional stenting and to select the size of the extra stent to treat residual plaque or edge dissection. |
| Final results should be primarily assessed by IVUS imaging, not angiography. |
| Restrict final angiography to 1 projection. There is no need for repeat angiography if good-quality IVUS imaging shows satisfactory results. |
| Consider not performing a final angiography in cases with a high confidence of optimal final results. |

IVUS = intravascular ultrasound; PCI = percutaneous coronary ultrasound.

Cumulative air kerma (measured in gray), cumulative dose-area product (measured in gray square centimeters), and the number of cine runs were prospectively collected as metrics for radiation dose. The duration of the intervention was estimated by the cumulative fluoroscopic time (in minutes) and by the procedure time (in minutes), defined as the time

**TABLE 3 Baseline and Procedural Characteristics**

| | Angiography Guided (n = 42 ) | IVUS Guided (n = 41) | p Value |
|---|---|---|---|
| Age, yrs | 62.1 (57.3–76.5) | 67.1 (58.3–76.1) | 0.3 |
| Male | 57.1 | 61.0 | 0.8 |
| Hypertension | 100 | 97.6 | 0.5 |
| Smoking status | | | 0.9 |
| Never | 59.5 | 58.5 | |
| Past | 33.3 | 36.6 | |
| Current | 7.1 | 4.9 | |
| Diabetes mellitus | 81.0 | 73.2 | 0.4 |
| Peripheral artery disease | 4.8 | 4.9 | >0.9 |
| Previous stroke | 4.8 | 12.2 | 0.3 |
| Previous CABG | 16.7 | 14.6 | >0.9 |
| Previous PCI | 11.9 | 26.8 | 0.1 |
| Clinical presentation | | | >0.9 |
| Silent ischemia or stable angina | 71.4 | 75.6 | |
| Acute coronary syndrome | 16.7 | 14.6 | |
| Ischemic equivalent* | 11.9 | 9.8 | |
| Serum creatinine, mg/dl | 1.1 (0.9–1.3) | 1.2 (0.9–1.5) | 0.4 |
| Creatinine clearance, ml/min/1.73 $m^2$ | 72.4 (47.2–89.9) | 60.5 (43.9–73.1) | 0.2 |
| Creatinine clearance <60 ml/min/1.73 $m^2$ | 40.5 | 48.8 | 0.5 |
| Treated vessel | | | |
| LMC | 7.1 | 4.9 | >0.9 |
| LAD | 52.4 | 34.1 | 0.1 |
| LCx | 28.6 | 46.3 | 0.1 |
| RCA | 35.7 | 22.0 | 0.2 |
| Graft | 2.4 | 9.8 | 0.2 |
| Lesion type | | | |
| A | 9.5 | 2.4 | 0.4 |
| B1 | 16.7 | 22.0 | 0.6 |
| B2 | 35.7 | 24.4 | 0.3 |
| C | 64.3 | 63.4 | >0.9 |
| Bifurcation lesion† | 26.2 | 24.4 | 0.5 |
| Moderate or severe calcification | 33.3 | 51.2 | 0.1 |
| Pre-dilation | 57.1 | 68.3 | 0.4 |
| No. of stents | 2.0 (1.0–2.3) | 2.0 (1.0–2.0) | 0.8 |
| Overlapping stents | 38.1 | 43.9 | 0.7 |
| Stent diameter, mm | 3.0 (3.0–3.5) | 3.0 (2.8–3.5) | 0.7 |
| Stent diameter ≤2.5 mm | 40.5 | 29.3 | 0.4 |
| Total sum of stent length, mm | 33.0 (22.3–54.5) | 32.0 (20.0–46.0) | 0.5 |
| Stent length ≥20 mm | 66.7 | 73.2 | 0.6 |
| Post-dilation | 78.6 | 95.1 | 0.048 |

Values are % or median (interquartile range). *Heart failure or arrhythmias documented related to myocardial ischemia. †Defined as a bifurcated target segment involving a side branch >2.0 mm in diameter.

CABG = coronary artery bypass graft surgery; LAD = left anterior descending artery; LCx = left circumflex artery; LMC = left main coronary; RCA = right coronary artery; other abbreviations as in Table 2.

from the first injection to the time the guiding catheter was removed.

The creatinine clearance was calculated based on the serum creatinine, using the equation proposed by Cockcroft and Gault (27). For all patients, sequential serum creatinine measurements were obtained on a daily basis during the index hospitalization. Post-PCI CI-AKI was defined as any increase in baseline serum creatinine values >0.5 mg/dl (28). A series of 25 consecutive patients with low creatinine clearance (<60 ml/min/1.73 $m^2$) undergoing angiography-guided PCI at our institution (unpublished data) was used as a basis for the sample size calculation. In that cohort, the average volume of contrast was 147.6 ± 66.8 ml. A sample size of 80 patients was found to be sufficient to show a significant reduction in the volume of contrast by 33% in the IVUS-guided group, assuming a similar SD for both study groups, with an alpha value of 0.05 and a beta value of 0.1. All analyses were carried out according to the intention-to-treat principle. Categorical variables and adverse events were presented as percentages and compared using the Fisher exact test or the chi-square test. Continuous variables were presented as median and interquartile range and compared using the Mann-Whitney *U* test. The incidence of post-discharge adverse events was estimated according to the Kaplan-Meier method and was compared between the groups using the log-rank test. All p values were 2-tailed and were considered significant if $p < 0.05$.

## RESULTS

Between November 2012 and September 2013, a total of 83 patients were randomly allocated to angiography-guided PCI (n = 42) or IVUS-guided PCI (n = 41). Patients' characteristics at baseline were similar between the study groups (Table 3). Overall, the vast majority of the patients had diabetes mellitus (77.1%), and most had stable coronary disease (73.5%). The median serum creatinine of the study population was 1.13 mg/dl (interquartile range [IQR]: 0.9 to 1.4 mg/dl), and 44.6% had a calculated creatinine clearance <66.0 ml/min/1.73 $m^2$. A median of 2.0 stents (IQR: 1.0 to 2.0 stents) were used, and most patients had complex target lesions (at least 1 type C lesion in 63.9% of patients).

**IODINE CONTRAST USE AND PROCEDURAL CHARACTERISTICS.** The total volume of contrast (study's primary endpoint) was 64.5 ml (IQR: 42.8 to 97.0 ml) (range, 19 to 170 ml) in the angiography-guided group versus 20.0 ml (IQR: 12.5 to 30.0 ml) (range, 3 to 54 ml) in the IVUS-guided group ($p < 0.001$) (Table 4). Similarly, the volume of contrast/creatinine clearance ratio was significantly different between the study groups (1.0 [IQR: 0.6 to 1.9] vs. 0.4 [IQR: 0.2 to 0.6], respectively; $p < 0.001$). Low-osmolar contrast media were used in all patients except 1 patient in the angiography-guided group who was treated with an iso-osmolar agent ($p > 0.9$). Slight

differences in indexes of renal function favored neither group and were statistically indistinguishable.

The procedure time of IVUS-guided PCI was significantly longer than angiography-guided interventions (median difference, 14.0 min; p = 0.006) (Table 4). However, the groups did not differ with regard to fluoroscopic time, number of cine runs, cumulative dose-area product, or cumulative air kerma (p ≥ 0.3 for all) (Table 4).

**IN-HOSPITAL AND POST-DISCHARGE OUTCOMES.** In-hospital outcomes during the index hospitalization were not different between patients randomized to angiography-guided or IVUS-guided PCI (Table 5). The peak serum creatinine in the angiography-guided PCI was 1.2 mg/dl (IQR: 1.0 to 1.5 mg/dl) versus 1.3 mg/dl (IQR: 1.0 to 1.6 mg/dl) in the IVUS-guided group (p = 0.4) (Table 5). Contrast-induced acute kidney injury (i.e., increase in serum creatinine >0.5 mg/dl) was diagnosed in 19.0% of patients treated with angiography-guided PCI and 7.3% of those randomized to IVUS-guided PCI (p = 0.2) (Table 5).

The median follow-up was 117 days (IQR, 45 to 177 days), there were no patients lost to follow-up, and all patients had at least 1 month of post-discharge follow-up. The incidence of death, myocardial infarction, unplanned revascularization, or stent thrombosis was not significantly different between the study groups (Table 5).

**TABLE 4 Iodine Contrast Use and Procedural Characteristics**

| | Angiography Guided (n = 42) | IVUS Guided (n = 41) | p Value |
|---|---|---|---|
| Total contrast volume, ml* | 64.5 (42.8–97.0) | 20.0 (12.5–30.0) | <0.001 |
| Volume of contrast per stent implanted, ml | 40.5 (25.7–48.3) | 13.0 (7.1–20.0) | <0.001 |
| Contrast volume/creatinine clearance ratio | 1.0 (0.6–1.9) | 0.4 (0.2–0.6) | <0.001 |
| Contrast volume/creatinine clearance ratio >2 | 19.0 | 4.9 | 0.09 |
| Procedure time, min | 34.0 (18.5–54.5) | 48.0 (34.0–61.0) | 0.006 |
| Fluoroscopy time, min | 12.2 (6.8–24.1) | 12.2 (8.4–20.8) | 0.5 |
| No. of cine runs | 22.5 (16.0–36.3) | 25.0 (19.0–32.5) | 0.5 |
| Cumulative DAP, Gy × $cm^2$ | 82.1 (54.5–132.0) | 73.7 (44.8–118.3) | 0.4 |
| Cumulative air kerma, Gy | 1.4 (1.0–2.7) | 1.4 (1.0–2.0) | 0.3 |

Values are % or median (interquartile range). *Primary endpoint.
DAP = dose-area product; IVUS = intravascular ultrasound.

## DISCUSSION

The main finding of the present study was that PCI performed primarily through IVUS imaging is safe and significantly reduces the dose of iodine contrast compared with an angiography-only approach. The mean contrast volume was 3-fold lower in the IVUS compared with the angiography arm. Both study groups were mainly composed of diabetic patients, frequently with long, calcified, bifurcated, and complex lesions, who often needed multiple stent implantation. It is of note that patients randomized to the angiography group also received a relatively low dose of contrast, particularly when considering such a high-risk population (24), given rigid contrast-saving strategies universally applied for the whole patient cohort, as suggested by Nayak et al. (20) and expanded in the present study. It must be highlighted, therefore, that the effects of IVUS guidance appeared to be an added benefit in contrast avoidance, in addition to already reduced contrast use.

IVUS was extensively used in the MOZART trial, almost as a substitute for angiography during PCI. Such an approach was proven safe, with no excessive use of additional stents or increase in the incidence of clinical adverse events. The IVUS-guided group had slightly but significantly longer procedures and greater use of stents post-dilation, even though no differences were noted in the number, length, or diameter of stents, as well as in fluoroscopy time, the number of cine runs, or radiation dose. Most probably the longer duration of IVUS-guided procedures resulted from IVUS acquisition and interpretation. This finding reinforces that specific IVUS training is needed to obtain the maximal results from the technology, as well as to imprint fluency to the procedure.

**TABLE 5 In-Hospital and 4-Month Outcomes***

| | Angiography Guided (n = 42) | IVUS Guided (n = 41) | p Value |
|---|---|---|---|
| In-hospital | | | |
| Death | 0 | 0 | – |
| Acute myocardial infarction† | 4.8 | 4.9 | >0.9 |
| Unplanned revascularization | 0 | 0 | – |
| Stent thrombosis | 0 | 0 | – |
| CK-MB increase >5× ULN | 11.9 | 14.6 | 0.8 |
| CK-MB peak, ng/ml | 2.4 (1.3–3.7) | 2.5 (1.1–9.4) | 0.5 |
| Peak serum creatinine, mg/dl | 1.2 (1.0–1.5) | 1.3 (1.0–1.6) | 0.4 |
| Lowest creatinine clearance, ml/min/1.73 $m^2$ | 61.9 (43.8–79.1) | 51.4 (40.5–72.9) | 0.3 |
| Peak increase in creatinine >0.5 mg/dl | 19.0 | 7.3 | 0.2 |
| 4-month post-discharge | | | |
| Death | 0 | 4.2 | 0.3 |
| Acute myocardial infarction‡ | 3.3 | 4.2 | >0.9 |
| Unplanned revascularization | 11.7 | 4.2 | 0.3 |
| Stent thrombosis | 0 | 0 | – |
| Any event | 11.7 | 4.2 | 0.3 |

Values are % or median (interquartile range). *Kaplan-Meier estimates. †All post-percutaneous coronary intervention. ‡All spontaneous.
CK-MB = creatine kinase-myocardial band; IVUS = intravascular ultrasound; ULN = upper limit of normal.

Over the past years, optical coherence tomography has been increasingly reported as an imaging tool to guide PCI. The relative advantages and disadvantages of optical coherence tomography over IVUS are yet to be established. The much higher spatial resolution of optical coherence tomography progressively established it as an important method for in vivo evaluation of lumen and plaque, as well as stent expansion, apposition, and tissue coverage. Current guidelines for the use of frequency-domain optical coherence tomography recommend intracoronary administration of contrast for blood cleaning during image acquisition. It is therefore improbable that the strategy and results reported in the present study could be directly extrapolated to contrast-based optical coherence tomography imaging. Intracoronary saline infusion could be explored as an alternative to contrast media, even though the safety and diagnostic accuracy of this approach have yet to be validated.

A number of previous randomized and observational studies evaluated the impact of IVUS guidance on the outcomes after coronary stent implantation, with recent meta-analytic data showing a significant decrease in the risk of adverse events (23). Our study was not designed or powered to detect differences in post-PCI renal function or clinical outcomes. Nevertheless, paralleling the decrease in contrast volume, patients treated with IVUS-guided PCI showed a numerically (nonsignificant) lower rate of post-PCI CI-AKI and adverse cardiac events after the index procedure. Trends in indexes of renal function that favor extensive IVUS use might likely emerge in larger and adequately designed studies.

**STUDY LIMITATIONS.** Patients were enrolled in the MOZART trial according to somewhat restricted criteria, which excluded patients with recent catheterization, using nephrotoxic agents, or with unstable or unknown renal function. Such a study population was selected mainly to reduce confounding factors in assessing the impact of contrast saving on post-procedure renal function and clinical outcomes. In fact, in real-world practice, those patients would also potentially benefit from IVUS guidance. It is possible that the increased interventional time and the use of IVUS catheters would increase the costs of IVUS-guided PCI. On the other hand, the reduction in contrast use and an eventual decrease in complications could potentially offset the increased costs. Further analysis in larger populations would be desirable to evaluate the cost-effectiveness profile of IVUS use in CI-AKI-prone patients undergoing PCI.

## CONCLUSIONS

Thoughtful and extensive use of IVUS as the primary imaging tool to guide PCI is safe and markedly reduces the volume of iodine contrast used compared with guidance by angiography alone. IVUS imaging should be considered for patients at high risk of CI-AKI or volume overload undergoing coronary angioplasty.

**REPRINT REQUESTS AND CORRESPONDENCE:** Dr. Pedro A. Lemos, Heart Institute (InCor), Service of Interventional Cardiology, Av. Dr. Eneas Carvalho de Aguiar, 44, Bloco I, 3° andar, Hemodinâmica, São Paulo-SP 05403-000, Brazil. E-mail: pedro.lemos@incor.usp.br.

## REFERENCES

**1.** James MT, Samuel SM, Manning MA, et al. Contrast-induced acute kidney injury and risk of adverse clinical outcomes after coronary angiography: a systematic review and meta-analysis. Circ Cardiovasc Interv 2013;6:37–43.

**2.** Solomon RJ, Mehran R, Natarajan MK, et al. Contrast-induced nephropathy and long-term adverse events: cause and effect? Clin J Am Soc Nephrol 2009;4:1162–9.

**3.** Hiremath S, Akbari A, Shabana W, Fergusson DA, Knoll GA. Prevention of contrast-induced acute kidney injury: is simple oral hydration similar to intravenous? A systematic review of the evidence. PLoS One 2013;8:e60009.

**4.** Chen Y, Hu S, Liu Y, et al. Renal tolerability of iopromide and iodixanol in 562 renally impaired patients undergoing cardiac catheterisation: the DIRECT study. EuroIntervention 2012;8:830–8.

**5.** Stone GW, McCullough PA, Tumlin JA, et al. Fenoldopam mesylate for the prevention of contrast-induced nephropathy: a randomized controlled trial. JAMA 2003;290:2284–91.

**6.** Jo SH, Koo BK, Park JS, et al. Prevention of radiocontrast medium-induced nephropathy using short-term high-dose simvastatin in patients with renal insufficiency undergoing coronary angiography (PROMISS) trial–a randomized controlled study. Am Heart J 2008;155:499.e1–8.

**7.** Majumdar SR, Kjellstrand CM, Tymchak WJ, Hervas-Malo M, Taylor DA, Teo KK. Forced euvolemic diuresis with mannitol and furosemide for prevention of contrast-induced nephropathy in patients with CKD undergoing coronary angiography: a randomized controlled trial. Am J Kidney Dis 2009;54:602–9.

**8.** Maioli M, Toso A, Leoncini M, Micheletti C, Bellandi F. Effects of hydration in contrast-induced acute kidney injury after primary angioplasty: a randomized, controlled trial. Circ Cardiovasc Interv 2011;4:456–62.

**9.** Kunadian V, Zaman A, Spyridopoulos I, Qiu W. Sodium bicarbonate for the prevention of contrast induced nephropathy: a meta-analysis of published clinical trials. Eur J Radiol 2011;79:48–55.

**10.** Sadat U, Usman A, Gillard JH, Boyle JR. Does ascorbic acid protect against contrast induced-acute kidney injury in patients undergoing coronary angiography—a systematic review with meta-analysis of randomized controlled trials. J Am Coll Cardiol 2013;62:2167–75.

**11.** Markota D, Markota I, Starcevic B, Tomic M, Prskalo Z, Brizic I. Prevention of contrast-induced nephropathy with Na/K citrate. Eur Heart J 2013;34:2362–7.

**12.** Er F, Nia AM, Dopp H, et al. Ischemic preconditioning for prevention of contrast

medium-induced nephropathy: randomized pilot RenPro Trial (Renal Protection Trial). Circulation 2012;126:296–303.

**13.** Sun Z, Fu Q, Cao L, Jin W, Cheng L, Li Z. Intravenous N-acetylcysteine for prevention of contrast-induced nephropathy: a meta-analysis of randomized, controlled trials. PLoS One 2013;8:e55124.

**14.** Mehran R, Aymong ED, Nikolsky E, et al. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. J Am Coll Cardiol 2004;44:1393–9.

**15.** Marenzi G, Assanelli E, Campodonico J, et al. Contrast volume during primary percutaneous coronary intervention and subsequent contrast-induced nephropathy and mortality. Ann Intern Med 2009;150:170–7.

**16.** Gurm HS, Dixon SR, Smith DE, et al. Renal function-based contrast dosing to define safe limits of radiographic contrast media in patients undergoing percutaneous coronary interventions. J Am Coll Cardiol 2011;58:907–14.

**17.** Tan N, Liu Y, Chen JY, et al. Use of the contrast volume or grams of iodine-to-creatinine clearance ratio to predict mortality after percutaneous coronary intervention. Am Heart J 2013;165:600–8.

**18.** Brown JR, Robb JF, Block CA, et al. Does safe dosing of iodinated contrast prevent contrast-induced acute kidney injury? Circ Cardiovasc Interv 2010;3:346–50.

**19.** Sayin T, Turhan S, Akyurek O, Kilickap M. Gadolinium: nonionic contrast media (1:1) coronary angiography in patients with impaired renal function. Angiology 2007;58:561–4.

**20.** Nayak KR, Mehta HS, Price MJ, et al. A novel technique for ultra-low contrast administration during angiography or intervention. Cathet Cardiovasc Interv 2010;75:1076–83.

**21.** Tunuguntla A, Daneault B, Kirtane AJ. Novel use of the GuideLiner catheter to minimize contrast use during PCI in a patient with chronic kidney disease. Catheter Cardiovasc Interv 2012;80:453–5.

**22.** Shinozaki N. A case of effective reduction in the amount of contrast medium using selective coronary angiography with a thrombus aspiration catheter. J Invasive Cardiol 2011;23:E232–4.

**23.** Sbruzzi G, Quadros AS, Ribeiro RA, et al. Intracoronary ultrasound-guided stenting improves outcomes: a meta-analysis of randomized trials. Arq Bras Cardiol 2012;98:35–44.

**24.** Wessely R, Koppara T, Bradaric C, et al. Choice of contrast medium in patients with impaired renal function undergoing percutaneous coronary intervention. Circ Cardiovasc Interv 2009;2:430–7.

**25.** Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. Circulation 2012;126:2020–35.

**26.** Serruys PW, Daemen J. Are drug-eluting stents associated with a higher rate of late thrombosis than bare metal stents? Late stent thrombosis: a nuisance in both bare metal and drug-eluting stents. Circulation 2007;115:1433–9; discussion 1439.

**27.** Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976;16:31–41.

**28.** Capodanno D, Ministeri M, Cumbo S, Dalessandro V, Tamburino C. Volume-to-creatinine clearance ratio in patients undergoing coronary angiography with or without percutaneous coronary intervention: implications of varying definitions of contrast-induced nephropathy. Catheter Cardiovasc Interv 2014;83:907–12.

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