Choice of Contrast Medium in Patients With Impaired Renal Function Undergoing Percutaneous Coronary Intervention

Rainer Wessely, MD; Tobias Koppara, MD; Christian Bradaric, MD; Marc Vorpahl, MD; Siegmund Braun, MD; Stefanie Schulz, MD; Julinda Mehilli, MD; Albert Schömig, MD; Adnan Kastrati, MD; for the Contrast Media and Nephrotoxicity Following Coronary Revascularization by Angioplasty (CONTRAST) Trial investigators

Background—No clinical trial has yet focused on contrast-mediated nephrotoxicity in patients with chronic renal failure exclusively undergoing percutaneous coronary intervention (PCI). Therefore, the aim of this study was to compare the effect of contemporary contrast media on nephrotoxicity in this high-risk patient population.

Methods and Results—This prospective, randomized, double-blind, comparative clinical trial randomly selected 939 patients with chronic renal failure undergoing coronary angiography with potential PCI to receive either the iso-osmolar contrast medium iodixanol or the low-osmolar contrast medium iomeprol. Of those 939 patients, 615 received diagnostic angiography only and were not included in the primary study analysis, but were followed up in a registry. Three hundred twenty-four patients underwent PCI, of which one-half received iodixanol or iomeprol, respectively, and were included in the primary study analysis. The primary end point was the peak increase in S-creatinine after PCI. Maximum increase in S-creatinine after PCI was lower than expected and thus impaired the power of the study. It was not significantly different between the 2 contrast groups (0.19±0.40 mg/dL for iodixanol and 0.21±0.34 mg/dL for iomeprol; P=0.53). Albeit contrast media–induced nephropathy rates were lower with iodixanol (22.2% compared with 27.8% for iomeprol), this difference was not statistically different (P=0.25). Subgroup analysis suggested a favorable outcome regarding nephrotoxicity in patients who received higher contrast volumes (>340 mL) in the iodoxanol group (Pinteraction=0.016).

Conclusions—Routine use of iso-osmolar contrast medium is not associated with a significant reduction of nephrotoxicity compared with low-osmolar contrast medium in patients with chronic renal failure undergoing PCI. However, a positive effect was seen in the iso-osmolar contrast group for patients receiving high amounts of contrast medium, which awaits confirmation of a specifically designed randomized clinical trial.

Clinical Trial Registration—clinicaltrials.gov Identifier: NCT00390585 (Circ Cardiovasc Intervent. 2009;2:430-437.)

Key Words: angioplasty ■ contrast media ■ kidney ■ chronic renal failure ■ contrast-induced nephropathy

Chronic kidney disease (CKD) carries an increased risk of death, cardiovascular events, and hospitalization.1 Even mild CKD is associated with worsened outcomes after myocardial infarction.2 Compared with the general population, patients with chronic renal failure are more likely to develop coronary artery disease (CAD)3 and exhibit an advanced disease stage at the time of primary diagnosis or coronary revascularization.4 Heart failure is associated with chronically impaired renal function irrespective of the presence of CAD.5 As is the case with coronary artery bypass grafting,6 the risk of percutaneous coronary intervention (PCI) is increased in patients with renal dysfunction and associated with impaired acute7 and long-term outcomes8 compared with the general population.

Clinical Perspective on p 437

Parenteral administration of iodized contrast medium is compulsory for PCI. Because patients with CKD reveal a higher frequency of diffuse disease and an increased rate of multivessel disease, applied contrast volumes are generally higher compared with regular patients.9

Although the incidence of contrast media–induced nephropathy (CIN) in patients with preserved renal function is very low,10 the risk for patients with risk factors such as
chronic renal failure and diabetes is considerably increased and ranges between approximately 12% and 50%. Importantly, it is elevated even in patients with moderate renal dysfunction. In addition to allergies, nephrotoxicity is a major side effect of intravascular administration of contrast media and is one of the leading causes of hospital-acquired renal failure. CIN is associated with increased cost and impaired acute and long-term outcome. Even mild impairment of renal function after PCI is independently associated with a significant increase in mortality after 5 years. The need for temporary or chronic renal replacement therapy as a sequel of CIN is even associated with a sharp increase in 1-year mortality. Therefore, prevention of CIN is warranted for improvement of renal and cardiovascular outcomes.

Risk factors for the development of CIN include diabetes mellitus, urgent versus planned PCI, congestive heart failure, older age, hypertension, hypotension, and, most importantly, CKD. Non–patient-related risk factors comprise properties of contrast media such as high- versus low osmolality as well as the volume of contrast medium delivered during coronary angiography.

Increased severity of CAD in patients with CKD often requires an elevated amount of contrast medium during complex PCI sessions. This fact may even exacerbate the already increased risk for CIN in patients presenting with chronically impaired renal function. Besides ionicity, contrast media are categorized according to their osmolality as so-called high-osmolar (osmolality >1000 mOsm/kg), low-osmolar (600 to 1000 mOsm/kg), and iso-osmolar (280 to 290 mOsm/kg) contrast media. Nowadays, high-osmolar contrast media have been replaced by low-osmolar and iso-osmolar contrast media because of better tolerability, lower side effects, and, importantly, a lower incidence of CIN. It is important to acknowledge that this classification, albeit commonly used, might be confusing because the so-called low-osmolar contrast media are in fact hyperosmolar compared with blood.

Conflicting data exist about the nephrotoxicity associated with the use of low-osmolar versus the use of iso-osmolar contrast media in patients with impaired renal function. Although some clinical trials and a meta-analysis suggest a lower incidence of CIN in patients receiving iso-osmolar contrast medium, some other prospective studies do not confirm these findings. Importantly, no prospective randomized trial is currently available that compared the effectiveness of iso-osmolar to low-osmolar contrast media exclusively in patients undergoing PCI who are exposed to high volumes of contrast medium.

Thus, the aim of the Contrast Media and Nephrotoxicity Following Coronary Revascularization by Angioplasty (CONTRAST) trial was to compare the nephrotoxic effects of the iso-osmolar contrast medium ioxithalamide with the low-osmolar contrast medium iopromide in patients with CKD undergoing PCI.

Methods

Study Patients

Patients with stable or unstable angina pectoris or a positive stress test undergoing coronary angiography with the possibility of PCI in a native vessel or bypass graft were eligible for this study if they were at least 18 years old and had impaired renal function with an estimated glomerular filtration rate (eGFR) of ≥60 mL/min/1.73 m² as determined by the Modification of Diet in Renal Disease (MDRD) formula or S-creatinine of ≥1.5 mg/dL, measured within 24 hours before coronary angiography. Criteria for exclusion were pregnancy, lactation, intravascular administration of iodine containing contrast medium within the previous 7 days, known allergies or incompatibilities to contrast media, concurrent intake of nephrotoxic drugs within the previous 7 days, renal transplantation, cardiogenic shock, end-stage renal disease necessitating hemodialysis, and inability to give informed consent to participate in the study. The study protocol was approved by an institutional ethics committee. All patients who were included in the trial gave written informed consent for participation in this study.

Study Protocol

Randomization was performed with sealed, opaque envelopes containing a computer-generated random sequence. Patients were randomly assigned to receive 1 of the 2 contrast mediums: the nonionic, iso-osmolar, dimeric contrast medium ioxithalamide (320 mg of iodine per milliliter; 290 mosm/kg of water [Visipaque, GE Healthcare Amersham Buchler]) or the nonionic, low-osmolar, monomeric contrast medium iopromide (350 mg of iodine per milliliter, 618 mosm/kg of water [Imeron, Altana Pharma]). To ensure blinding, bottles of contrast media identical in volume were placed into an opaque retaining bracket so that invasive cardiologists were not aware of the type of contrast medium. Both contrast media were supplied and kept at 37°C throughout the procedure. All patients received intravenous hydration before contrast exposure. It was recommended to receive 1 mL NaCl 0.9%/kg body weight for 12 hours before and after contrast exposure unless clinical or logistic circumstances did not allow for this. Because of inconsistent results concerning the role of acetylcysteine to prevent CIN, its use was not recommended. Thus, no patient included in the study received acetylcysteine or other potential pharmacological agents to impact on the incidence of CIN.

The primary end point of the study was the peak increase of S-creatinine as a measure of contrast medium–induced nephrotoxicity during hospitalization for PCI. Specifically, S-creatinine was assessed on a daily basis at least until the value after PCI was equal or less than the baseline value determined before PCI. Secondary end points were incidence of CIN (defined by a increase in creatinine ≥0.5 mg/dL or 25% of the initial value), severe CIN (defined by an increase in S-creatinine by ≥1 mg/dL and/or dialysis), and duration of hospitalization. Major adverse cardiac events (death, myocardial infarction, and target lesion revascularization) were assessed at 6 months. The follow-up protocol included a phone interview at 30 days and a 6-month visit.

Patients receiving diagnostic coronary angiography only were followed up separately for reasons of completeness in a registry. Follow-up of these patients included routine assessment of peak S-creatinine levels during hospitalization as well as a telephone interview at 6 months.

Statistical Analysis

The peak increase of S-creatinine in patients who received low-osmolar contrast media varies considerably in previous studies that included patients undergoing coronary angiography. This is exemplified in 2 of the most recognized trials in the field. Although the CARE study reported a mean peak increase in S-creatinine of 0.07 mg/dL, NEPHRIC accounted a mean peak increase of 0.55 mg/dL. Because we expected a higher peak increase than the mean value of these numbers in our study that comprised patients who were expected to receive higher volumes of contrast media because of PCI, the sample size of the CONTRAST trial was calculated assuming a mean increase in S-creatinine levels of 0.4 mg/dL after PCI in the iopromide group, at least 25% less increase with ioxithalamide, a 2-sided α level of 0.05, and 90% power. Baseline and sequential S-creatinine measurements were determined in the identical laboratory for clinical chemistry located in each hospital. A total sample size of 286 patients was calculated on the basis of these
assumptions. Because the performance of PCI could not be predicted before diagnostic coronary angiography, the design of the study required randomization of a larger number of patients to allow for the inclusion of the needed number of patients who received PCI (Figure 1). Because randomization was performed before diagnostic angiography, several adjustments in the group assignment ratio were performed to achieve an equal number of patients with PCI in each of the study arms.

Baseline descriptive statistics are presented as frequencies and percentages for categorical variables and means ± SD or median (interquartile range) for continuous variables. Intergroup comparisons were assessed using Student t test (continuous data) and χ² or Fisher exact test (where expected cell value was <5) for categorical variables. Survival and event-free status were assessed using the methods of Kaplan–Meier and the log-rank test. Statistical software S-PLUS, version 4.5 (S-PLUS, Insightful Corp, Seattle, Wash) was used for all analyses.

Results

From June 2006 to December 2007, a total of 324 patients were enrolled in this trial: 162 patients received ioxaglate and 162 patients received iomeprol (Figure 1). Baseline characteristics, as depicted in Table 1, were equally distributed between the 2 groups. Compared with typical PCI populations, patients with CKD included in the CONTRAST study reflected a more complex study population with advanced age, a relatively high frequency of diabetes, and a high incidence of concomitant atherosclerotic risk factors such as hypertension and hyperlipidemia.

The high cardiac risk profile was reflected by the complexity of CAD. The high proportion of patients having multivessel disease and 78% of patients presenting with complex lesions. Multiple lesions were treated in >40% of the cases (Table 2). Procedural characteristics for PCI patients were similar and not statistically different in both contrast groups as shown in Table 3.

Renal function was similar for both contrast groups with an eGFR of 46.4 ± 9.3 mL/min/1.73 m² in the ioxaglate group and 47.1 ± 9.0 mL/min/1.73 m² in the iomeprol group, P = 0.44 (Table 2). Distribution of eGFR is depicted in Figure 2. Average hydration time before exposure to contrast medium was 6.3 hours for patients receiving ioxaglate and 6.5 hours for patients receiving iomeprol (P = 0.59). Mean contrast volume delivered during the entire procedure was not significantly different between the 2 groups (ioxaglate, 366 ± 158 mL; iomeprol, 367 ± 170 mL; P = 0.93).

The mean change of S-creatinine post-PCI was not significantly different between the groups and amounted to 0.19 ± 0.40 mg/dL in the ioxaglate group and 0.21 ± 0.34 mg/dL in the iomeprol group (P = 0.53). This translated to a 12.6 ± 25.8% and 16.1 ± 24.7% increase (P = 0.20), respectively, compared with the index value. Both the rates of CIN (ioxaglate, 22.2%; iomeprol, 27.7%; P = 0.25) and severe CIN (ioxaglate, 6.2%; iomeprol, 3.7%; P = 0.30) and the need for postinterventional hemodialysis were not statistically different between the groups (Table 4; Figure 3). This translated into a similar duration of hospitalization for PCI (ioxaglate, 6.3 ± 4.9 days; iomeprol, 6.5 ± 4.4 days; P = 0.59).

Figure 4 (A and B) illustrates the impact of ioxaglate on the primary end point in the prespecified PCI subgroups defined by the presence of diabetes, baseline renal function and quantity of contrast medium used during the procedure. No significant interaction was found between the type of contrast medium and diabetes (Pinteraction = 0.12) or eGFR (Pinteraction = 0.14), respectively. Contrarily, there was a significant interaction between the type and quantity of contrast medium used during the procedure (Pinteraction = 0.016) in the sense that ioxaglate was more favorable in terms of prevention of nephrotoxicity in patients who received higher amounts of contrast media (>340 mL) (Figure 4A).

Clinical follow-up was available for 99.4% of the study population at 6 months (Table 5). No significant differences were detected between the 2 groups regarding 6-month adverse outcomes. The curves of the composite major adverse
in patients who received solely coronary angiography was shown to be associated with favorable in-hospital and long-term survival rates.14 Thus, there is a high clinical need to decrease the incidence of CIN.17 On the other hand, the prevention of CIN itself put these patients at increased risk for contrast-mediated nephrotoxicity.18 In addition, patients who received solely coronary angiography had a marginally better renal function compared with PCI patients with no significant difference between the iodixanol group (eGFR = 49.2 ± 13.0 mL/min/1.73 m²) and the iomeprol group (eGFR = 49.1 ± 10.9 mL/min/1.73 m²), P = 0.84 (supplemental Table III). Contrast volumes were similar in patients who received diagnostic coronary angiography only (iodixanol, 146 ± 58 mL; iomeprol, 144 ± 53 mL; P = 0.57). Compared with PCI patients, those undergoing diagnostic coronary angiography only showed a lower incidence of maximal peak increase in S-creatinine after contrast exposure (iodixanol, 0.08 ± 0.29 mg/dL; iomeprol, 0.06 ± 0.27 mg/dL; P = 0.47), CIN (iodixanol, 9.2%; iomeprol, 8.0%; P = 0.59) as well as severe CIN (iodixanol, 1.0%; iomeprol, 1.2%; P = 0.77). The 6-month rate for myocardial infarction and death was similar in both groups (supplemental Table IV).

### Discussion

The CONTRAST study is the first trial that was conducted to exclusively assess the outcomes of patients with CKD undergoing PCI with regard to contrast-mediated nephrotoxicity. The presence of chronic renal failure, its associated cardiovascular risk factors, advanced CAD, and the PCI procedure itself put these patients at increased risk for contrast-mediated nephrotoxicity.17 On the other hand, the prevention of CIN after PCI has been shown to be associated with favorable in-hospital and long-term survival rates.14 Thus, there is a high clinical need to decrease the incidence of CIN.

Although there is general consensus that low-osmolar contrast media are superior to high-osmolar contrast media, in particular, in terms of nephrotoxicity,11,18 conflicting data have been reported in clinical trials comparing low-osmolar with iso-osmolar contrast media for prevention of nephrotoxicity in mixed patient populations receiving angiography but only partially undergoing PCI.
Overall, we found no significant difference between the mean peak increase of S-creatinine and CIN after PCI between the iso-osmolar iodixanol group and the low-osmolar iomeprol group. As expected, patients receiving diagnostic coronary angiography only who were followed up outside the clinical trial showed considerably lower levels of nephrotoxicity, emphasizing the fact that the amount of contrast medium and the PCI procedure itself have a major impact on the increased rate of nephrotoxicity that was observed in the study population.

Patients randomly assigned to the CONTRAST study can be considered a high-risk population in terms of renal and cardiovascular outcome. Because laboratory assessment of renal function by measurement of S-creatinine and eGFR was mandatory before study enrollment, most patients had stable CAD. The high-risk profile of CONTRAST study patients receiving PCI is exemplarily reflected by advanced age with an average of 74.1 years, impaired ejection fraction with a mean of 50.4%, and a high incidence of multivessel disease that affected \( \approx 9 \) of 10 patients.

The high incidence of multivessel disease translated into a need for increased contrast volumes during PCI. The average contrast volume delivered for diagnostic angiography immediately following coronary intervention was 367 mL, which is in good accordance with the COURT trial that studied the impact of different contrast media on the incidence of major adverse cardiac events after PCI.\(^9\) Other trials that included a significant portion of patients solely undergoing coronary angiography without PCI reported the use of lower amounts of contrast media, such as in NEPHRIC\(^{11} \) (\( \approx 163 \) mL), RECOVER\(^{22} \) (\( \approx 200 \) mL), and CARE\(^{23} \) (\( \approx 135 \) mL).

Because CONTRAST is a unique clinical trial regarding study population that comprised patients undergoing PCI only, its outcome cannot be readily compared with that of other trials. The incidence of CIN varies significantly between numerous studies. Despite lower amounts of contrast media delivered, most trials reported CIN rates for low-osmolar contrast media comparable with those observed in the CONTRAST trial;\(^{11,18,22,26–29} \) however, some studies have reported a lower incidence of CIN.\(^{23,30} \) Similarly, a CIN rate
iodixanol use compared with a low-osmolar contrast medium significantly lower incidence of nephrotoxicity associated with CIN in the ICON study with 16.2%; however, the CIN rate for the identical contrast medium was only 3% in the NEPHRIC trial, which included exclusively patients with chronic renal failure and concomitant diabetes undergoing coronary angiography, but of which only ~20% underwent PCI.

Overall, CIN rates reported in the CONTRAST trial seem higher than in most other trials that assessed the nephrotoxicity associated with the use of contrast media in cardiovascular medicine. This can be readily explained by both the high-risk study population and the fact that all patients in this trial underwent PCI that is associated with considerably higher volumes of contrast than mere diagnostic coronary angiography. Presence of chronic renal failure and concomitant PCI increase the risk for contrast-mediated nephrotoxicity considerably. Heterogeneity in study population and delivered contrast volumes are most likely to account primarily for the divergent results among clinical contrast trials available so far that did not require obligatory PCI for inclusion into the clinical study.

There is general consensus that intravenous hydration has an important role for CIN prevention. However, no additional pharmacological therapy is consistently associated with improved outcomes after contrast exposure. Therefore, the CONTRAST study protocol required intravenous hydration before and after contrast exposure but discouraged the use of drugs, such as acetylcysteine, fenoldopam, theophylline, to strengthen clinical results. Thus, none of these drugs was given to any of patients of this trial. In addition, nephrotoxic drugs, such as metformin, aminoglycosides, or nonsteroidal anti-inflammatory drugs, had to be stopped at least 7 days before cardiac catheterization.

In terms of cardiovascular end points, 6-month follow-up revealed no differences regarding death and myocardial infarction. However, there was a weak trend toward a lower need for target vessel revascularization in the iodixanol group (3.1% versus 6.2% for iomeprol; _P_ = 0.19) and overall major adverse coronary events (8.6% versus 13.0%; _P_ = 0.21). This observation can be regarded as hypothesis generating and needs to be addressed in a dedicated clinical trial. In this context, it should be acknowledged that the COURT trial reported a lower major adverse coronary event rate at 30 days in patients who received iodixanol undergoing PCI.

Formerly, the NEPHRIC study that included exclusively diabetic patients with impaired renal function found a significantly lower incidence of nephrotoxicity associated with iodixanol use compared with a low-osmolar contrast medium after coronary angiography. Therefore, we conducted a pre-specified subgroup analysis for diabetic patients. However, in the diabetic patient population of the CONTRAST trial, we could not detect a significant difference between the investigated contrast media.

Yet, patients who received higher amounts of contrast medium than the median of 340 mL revealed less nephrotoxicity when they received iodixanol compared with iomeprol (_P_ interaction = 0.016). This suggests that the use of an iso-osmolar contrast medium might be a valid option in patients with impaired renal function who are expected to receive increased contrast volumes for PCI.

Given the highly complex patient background, the increased contrast volumes needed for diagnostic and therapeutic coronary angiography, and the results of previous clinical trials that investigated the effect of lower contrast volumes in study populations with only a fraction undergoing PCI, the data of the CONTRAST study may hint to a ceiling effect regarding the efficacy of different contrast media for the prevention of contrast medium–related renal dysfunction after PCI. This is consistent with subgroup analysis that suggests that patients who receive a high amount of contrast volume may still profit from iso-osmolar contrast media. These findings also implicate that contrast exposure should be limited to a minimum in patients with chronic renal failure undergoing PCI and that physicians should be open to staged procedures, although they might be more demanding in terms of patient compliance and costs.

### Limitations of the Study

Although this is the largest randomized trial examining the impact of iso-osmolar contrast media compared with low-osmolar contrast media in patients with impaired renal function undergoing PCI on nephrotoxicity, the sample size was still limited to enable careful evaluation of clinical end points. CONTRAST used a common primary end point, the increase in _S_-creatinine after exposure to contrast media. Although various studies have shown that there is a link between the increase of _S_-creatinine as marker of renal function and clinical outcome, it should be emphasized that _S_-creatinine is still a surrogate marker. In addition, interpret-
ing the results of subgroup analyses should be considered as hypothesis generating. Although the trial was carefully planned according to the existing literature, the primary end point was lower than expected and thus weakened the power of the trial.

In conclusion, the CONTRAST trial revealed that routine use of iso-osmolar contrast medium is not associated with a significantly lower degree of nephrotoxicity compared with the use of low-osmolar contrast medium. However, certain subgroups, such as patients who are expected to receive a high amount of contrast medium, may benefit from the use of the iso-osmolar contrast medium iodixanol. However, this awaits confirmation by a dedicated clinical trial. Further studies are needed to define the role of divergent contrast media in this or other high-risk patient subgroups.

Appendix


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Disclosures

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References

Impaired renal function is frequently associated with coronary artery disease, which in turn has a negative impact on the prognosis of patients with chronic renal failure. Revascularization by percutaneous coronary intervention is an effective treatment of coronary artery stenosis. However, it requires the use of iodinated contrast medium that can lead to acute renal failure, in particular in patients with underlying impaired renal function, termed contrast-induced nephropathy. Iodinated contrast media are grouped by their osmolality. Iso-osmolar contrast medium, such as ioxaglate, resembles the osmolality of blood, whereas all other commercially available contrast media, such as iomeprol, exhibit higher osmolality. The findings of the contrast study that randomly assigned patients undergoing percutaneous coronary intervention to receive either ioxaglate or iomeprol suggest that iso-osmolar contrast medium does not exhibit significantly lower nephrotoxicity compared with higher-osmolar contrast medium in unselected patients with chronic renal dysfunction. However, subgroup analysis suggested decreased nephrotoxicity in patients who received high contrast volumes favoring iso-osmolar contrast medium. Considering the results of the Contrast Media and Nephrotoxicity Following Coronary Revascularization by Angioplasty study as well as a recent meta-analysis and other randomized clinical trials that compared iso-osmolar with higher-osmolar contrast medium in mixed patient cohorts undergoing coronary angiography, iso-osmolar contrast medium should be considered as a first-line option for use in this high-risk patient population.
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Supplemental Material

Supplemental material does exclusively consist of supplementary tables.
Supplementary Table S1

Baseline and clinical characteristics of patients receiving diagnostic cardiography only

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Iodixanol group (n = 315)</th>
<th>Iomeprol group (n = 336)</th>
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<tr>
<td>Age – yr</td>
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<td>Men – n, (%)</td>
<td>208 (66)</td>
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<td>Diabetes mellitus – n, (%)</td>
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<td>IDDM – n, (%)</td>
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<td>History of smoking – n, (%)</td>
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<td>120 (36)</td>
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<td>Arterial hypertension – n, (%)</td>
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<td>306 (91)</td>
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<td>Hypercholesterolemia – n, (%)</td>
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<td>Prior myocardial infarction – n, (%)</td>
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<td>Prior aortocoronary bypass surgery – n, (%)</td>
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<td>Ejection fraction – (%)</td>
<td>50.8 ± 12.7</td>
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Medication on admission

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<td>ACE Inhibitor – n, (%)</td>
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<td>Statin – n, (%)</td>
<td>264 (84)</td>
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**Supplementary Table S 2**

**Baseline angiographic characteristics of patients receiving solely diagnostic cardangiography and not undergoing PCI**

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<th>Iomeprol group (n = 336)</th>
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<tr>
<td><strong>Diseased vessels</strong></td>
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<td>- 1-vessel disease – n. (%)</td>
<td>45 (14)</td>
<td>52 (15)</td>
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<td>- 2-vessel disease – n. (%)</td>
<td>60 (19)</td>
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<td>- 3-vessel disease – n. (%)</td>
<td>155 (49)</td>
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**Supplementary Table S3**

**Renal function before and after contrast exposure in patients receiving solely diagnostic cardangiography**

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<th>Iomeprol group (n = 336)</th>
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<td>S-Creatinine prior PCI – [mg/dl]</td>
<td>1.33 ± 0.41</td>
<td>1.29 ± 0.30</td>
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<td>S-Urea prior PCI – [mg/dl]</td>
<td>55.4 ± 27.7</td>
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<td>eGFR – [ml/min*1.73m²]</td>
<td>49.2 ± 13.0</td>
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<td>.86</td>
</tr>
<tr>
<td>Volume contrast media delivered – [ml]</td>
<td>146 ± 58</td>
<td>144 ± 53</td>
<td>.57</td>
</tr>
<tr>
<td>Maximal S-Creatinine post PCI – [mg/dl]</td>
<td>1.41 ± 0.61</td>
<td>1.35 ± 0.43</td>
<td>.20</td>
</tr>
<tr>
<td>Maximal S-Urea post PCI – [mg/dl]</td>
<td>56.0 ± 26.5</td>
<td>54.1 ± 27.0</td>
<td>.32</td>
</tr>
<tr>
<td>Maximal rise in S-Creatinine – [mg/dl]</td>
<td>0.08 ± 0.29</td>
<td>0.06 ± 0.27</td>
<td>.47</td>
</tr>
<tr>
<td>Maximal rise in S-Creatinine – [% of prior PCI]</td>
<td>5.0 ± 15.9</td>
<td>4.9 ± 17.9</td>
<td>.95</td>
</tr>
<tr>
<td>Maximal rise in S-Urea – [mg/dl]</td>
<td>0.60 ± 15.0</td>
<td>0.51 ± 12.7</td>
<td>.94</td>
</tr>
<tr>
<td>Hemodialysis post PCI – n, (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>NA</td>
</tr>
<tr>
<td>CIN – n, (%)</td>
<td>29 (9.2)</td>
<td>27 (8.0)</td>
<td>.59</td>
</tr>
<tr>
<td>Rise in S-Creatinine ≥ 1 mg/dl – n, (%)</td>
<td>3 (1.0)</td>
<td>4 (1.2)</td>
<td>.77</td>
</tr>
</tbody>
</table>
Supplementary Table S4.

Clinical 6-months follow-up of patients receiving solely diagnostic cardangiography

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Iodixanol group (n = 315)</th>
<th>Iomeprol group (n = 336)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction – n, (%)</td>
<td>1 (0.3)</td>
<td>0 (0)</td>
<td>.30</td>
</tr>
<tr>
<td>Death – n, (%)</td>
<td>18 (5.7)</td>
<td>16 (4.8)</td>
<td>.59</td>
</tr>
</tbody>
</table>