CARDIOLOGIE TUNISIENNE

ARTICLE ORIGINAL

Iodixanol versus Iopromide in patients at high risk for contrast induced nephropathy: IO2 contrast study

Iodixanol versus Iopromide chez les patients à haut risque de néphropathie induite au produit de contraste: Etude IO2 contrast

Lobna Laroussi[1,2], Afef Ben Halima[1,2], Ahmed Houmed, Emna Bennour[1,2], ZiedIBn El Haj[1,2], Marouene Boukhris[1,2], Ikram Kammoun[1,2], Faouzi Addad[1,2], Sonia Marrakchi[1,2], Salem Kachboura[1,2]

1. University of Tunis El Manar, Faculty of Medicine, 1006, Tunis, Tunisia
2. AbderrahmenMami Hospital, department of cardiology, 2080, Tunis, Tunisia,

Résumé

Introduction : La supériorité en termes de tolérance rénale des produits de contraste iodés (PDCI) iso-somolaires par rapport à ceux d'osmolarité basse, chez les patients à risque de néphropathie induite au produit de contraste (NIPC) demeure un sujet de controverse.

Objectifs: Nous nous sommes proposés de comparer l'impact sur la fonction rénale de ces deux types de PDCI chez des sujets à risque de NIPC.

Méthodes: Nous avons mené une étude prospective randomisée monocentrique chez des patients avec une indication à une coronarographie et/ ou une angioplastie transcutanée (ATC), et ayant un risque de NIPC allant d'intermédiaire à très élevé (score de Mehran ≥6). Les patients ont été randomisés (1:1) en 2 groupes selon le PDCI: Iopromide, Ultravist® [Bayer] (PDCI d'osmolarité basse) vs. Iodixanol, Visipaque® [GE HEALTHCARE] (PDCI iso-osmolaire). Un dosage de la créatinémie a été réalisé à l'état de base et 48-72h après la procédure. La NIPC a été définie par une augmentation de 44μmol/l (0.5mg/dl) en valeur absolue de la créatininémie ou une augmentation de plus de 25% de la créatinine de base 48 à 72h suivant l'injection de PDCI.

Résultats: Au total, 102 patients (51 dans chaque groupe) ont été inclus dans l'étude. Il n'existait pas de différence significative entre le groupe Iopromide et le groupe Iodixanol à l'exception de la créatininémie (157.1±36 vs. 181.5±55.7 μmol/l; p=0.01), alors que la clairance de la créatinine (37.2±10.8 vs. 34.2±10.2 ml/min; p=0.147) et le score de Mehran (9.2 ± 2.4 vs. 9.9 ± 2.6; p=0.168) étaient comparables entre les deux groupes. Pour le volume de PDCI utilisé, un trend a été observé pour le groupe Iopromide vs. Iodixanol (63.6±36.7 vs. 51.2±2.9ml; p=0.077). Neuf patients ont présenté une NIPC soit une incidence globale de 8.8%. Il n'existait pas de différence significative entre le groupe Iopromide et le groupe Iodixanol (7.8 vs. 9.8%; p=0.727). Aucun cas décès ou de recours à la dialyse en intra-hospitalier et à 3 mois, n'a été observé dans les 2 groupes.

Conclusion : Nos résultats montrent une bonne tolérance rénale équivalente entre l'Iopromide et l'Iodixanol chez les patients à risque de NIPC allant d'intermédiaire à très élevé.

Mots-clés
Produit de contraste, insuffisance rénale aigue, angiographies coronaires

Summary

Background: The superiority of iso-osmolar contrast agents (CA) in comparison with those low osmolar, in patients with high risk of contrast induced nephropathy (CIN) remains debatable through literature.

Objectives: We sought to assess the renal impact of these two types of CA in patients with high risk of CIN.

Methods: We performed a prospective randomized monocentric study, including patients with moderate to high risk of CIN (defined as Mehran score ≥6), undergoing coronary angiography and/or percutaneous coronary intervention (PCI). Patients were enrolled in a 1:1 fashion into 2 groups according to the CA: Iopromide, Ultravist® [Bayer] (low osmolar CA) vs. Iodixanol, Visipaque® [GE HEALTHCARE] (iso-osmolar CA). Serum level of creatinine was measured at baseline and 48-72h after the procedure. CIN was défined as an increase ≥44μmol/l (0.5mg/dl) or ≥25% in baseline creatinine serum level 48 -72h following the procedure.

Results: A total of 102 patients (51 in each group) were enrolled into the study. No difference was observed in baseline patients characteristics between Iopromide group and Iodixanol group except in baseline creatinine serum level (157.1±36 vs. 181.5±55.7 μmol/l, respectively; p=0.01), whereas creatinine clearance (37.2±10.8 vs. 34.2±10.2 ml/min; p=0.147) as well as Mehran score (9.2 ± 2.4 vs. 9.9 ± 2.6; p=0.168) were similar between the two groups. Regarding contrast load, a trend was observed in Iopromide group vs. Iodixanol group (63.6±36.7 vs. 51.2±2.9ml; p=0.077). Nine patients experienced CIN for an overall incidence of 8.8%. No difference in CIN occurrence was found between the two groups (7.8 vs. 9.8%; p=0.727). No death or need for dialysis was noticed during in-hospital stay or at 3-month follow up in both groups.

Conclusions: Our data showed a comparable satisfactory renal tolerance of Iopromide and Iodixanol in patients with moderate to very high risk of CIN.

Keywords
Contrast agents, acute renal failure, coronary angiography

Correspondance
Dr Lobna Laroussi
Abderrahmen Mami Hospital, department of cardiology, 2080, Tunis, Tunisia
email: Lobna_laroussi@hotmail.com

INTRODUCTION

Diagnostic and therapeutic contrast media-based procedures are increasingly carried out [1]
Contrast media (CM) is the third most common cause of hospital-acquired acute kidney injury (AKI), and coronary coronarography or angioplasty accounts for the highest incidence of contrast induced AKI (CI-AKI) [2]. Many individual risk factors for the development of CIN have been reported [3, 4] including advanced age, diabetes mellitus (DM), congestive cardiac failure (CCF), and chronic kidney disease (CKD) [2]. All these risk factors are highly prevalent in patients with coronary artery disease. Individual patient risk for contrast induced nephropathy (CIN) was globally assessed with the calculation of a simple risk score based on readily available information: mehran risk score [5].
Thus, numerous CI-AKI preventive strategies have been employed, such as reduced CM load and avoidance of recurrent exposure [6], intravascular volume expansion [7], N-acetylcysteine administration [8], and preferred use of iso-osmolar CM (IOCM) or low-osmolar CM (LOCM) over high-osmolar CM (HOCM) [9].
In the present study, we compared the renal effects of the nonionic, isoosmolar CM (IOCM), iodixanol versus the non-ionic, low-osmolar CM (LOCM), iopromide in high risk patients by evaluating the incidence of CIN.

METHODS

Study population

We performed a prospective randomized monocentric study, including 102 patients undergoing coronary angiography and/or percutaneous coronary intervention (PCI) at cardiology department of Abderrahmen Mami Hospital, Ariana between January 2015 and December 2016.
The Inclusion criteria were patients over 18 years old with moderate to high risk of CIN (defined as Mehran score ≥6).
The non-inclusion criteria were as follows: recent alteration of renal function in pre-procedure, intravenous administration of contrast agent (CA) in the week prior to inclusion, known allergy to the used CA, acute coronary syndrome with persistent ST segment elevation, cardiogenic shock state, end-stage renal failure (defined as a clearance of creatinine<10 ml / min) or dialysis.
All patients signed informed consent.

Variables and definitions

The contrast-induced nephropathy (CIN) was defined as a post-dose absolute increase in serum creatinine (SCr) of ≥ 0,5 mg/dl from baseline or a relative increase of 25%.measured at day 2 or 3.

Based on the definitions used in the Mehran CIN risk score [5], ''anemia'' was defined using World Health Organization criteria: baseline hematocrit value <39% for men and <36% for women. ''Chronic kidney disease'' was defined as an estimated glomerular filtration rate (eGFR) of <60 ml/min/1.73 m^2 (Levey modified MDRD formula). ''Hypotension'' was systolic blood pressure <80 mmHg for at least 1 h requiring inotropic support with medications or intra-aortic balloon pump (IABP) within 24 h peri-procedural.

Calculation of the Mehran CIN risk score

The final Mehran CIN risk score was calculated for each patient from the corresponding scores for the 8 prognostic variables it involves [Fig. 1]. Four categories of risk of CIN were established from the cut-off points and intervals defined by Mehran et al. as follows: low, 5 points; moderate, 6 to 10; high, 11 to 15; and very high, >15.

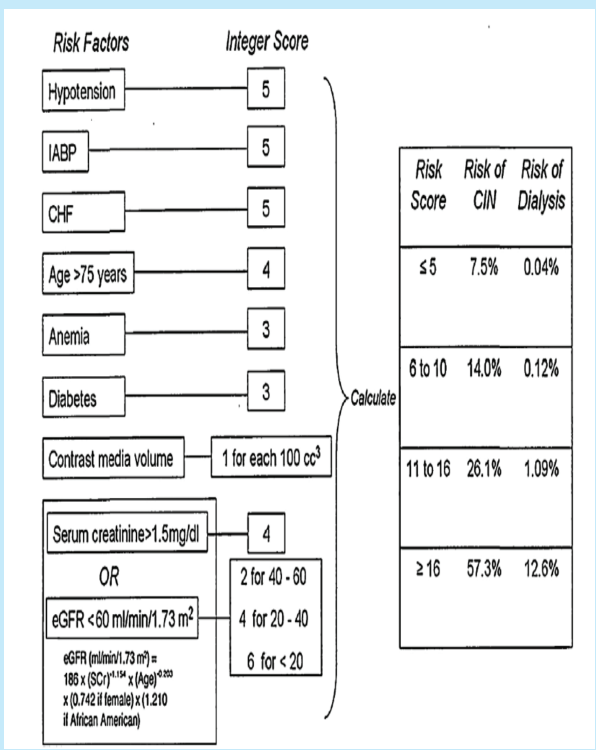

Figure 1: Mehran contrast-induced nephropathy risk score

Study protocol

The study was performed in accordance with the Declaration of Helsinki. All patients gave written informed consent before enrollment. The protocol of our study is shown in figure 2.

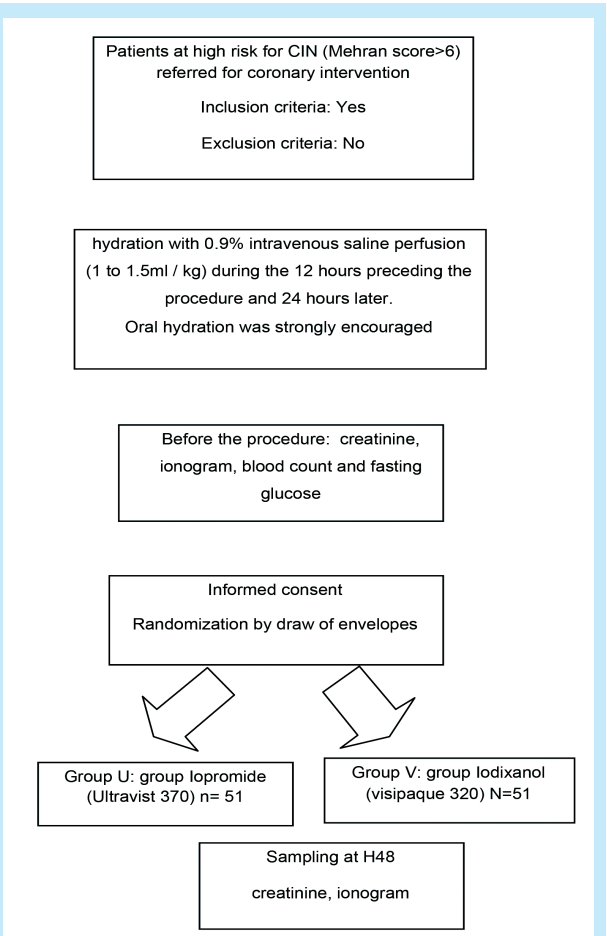

Figure 2 : The study protocol

Study End Points

The primary endpoint was the occurrence of CIN with an increase of 44 µmol / l (0.5 mg / dl) in absolute creatinine or an increase of more than 25% in baseline creatinine measured 48 to 72 hours after contrast administration.

The secondary endpoints were:

- The difference between initial and final absolute values of serum creatinine and creatinine clearance
- Intra-hospital mortality
- The use of intra-hospital dialysis.

Statistical Analysis

Continuous variables were expressed as the mean plus or minus standard deviation, and quantitative variables were expressed as percentages. Variables were compared using Student's t test for quantitative variables and the chi-squared test for qualitative variables; a value of p≤0.05 was considered to be significant.

RESULTS

The study population's characteristics

Between January 2015 and December 2016, 187 patients at high risk for CIN (Mehran score>6) were referred for diagnostic angiography with or without PCI.

After exclusions, data from 102 patients (51 in each arm) were available for analysis. Both groups were similar with respect to baseline demographics and clinical characteristics.

Biological characteristics were also similar with the exception of serum creatinine (157.1 ± 36 in the iopromide group vs. 181.5 ± 55.7 µmol / l in the iodixanol group, p = 0.01), whereas creatinine clearance was comparable between the two groups (37.2 ± 10.8 vs. 34.2 ± 10.2 ml / min p = 0.147) [Table 1].

Table 1: Demographic and clinical characteristics of the study population

	General population (N=102)	Group U (N=51)	Group V (N=51)	p
Mean age ±SD, years	68.9±11.8	69.3±10.8	68.6±12.8	0.764
Age ≥70 years, n(%)	54(52.9%)	27(52.9%)	27(52.9%)	1
Male sex, n(%)	73(71.6%)	34(66.7%)	39(76.5%)	0.315
Diabetes mellitus, n(%)	69 (67.6%)	31 (60.8)	38 (74.5%)	0.138
Hypertension, n(%)	85(83.3%)	45(88.2%)	40(78.4%)	0.184
Smoking, n(%)	42(41.2%)	19(37.3%)	23(45.1%)	0.421
Dyslipidemia, n(%)	85(83.3%)	85(83.3%)	85(83.3%)	0.185
LVEF, % mean ± SD	47.3±13.5%	49.7±13.5%	45.1±13.5%	0.084
LVEF <40%, n(%)	31(30.4%)	13(27.5%)	18(35.3%)	0.282
Heart failure, n (%)	41(40.2%)	18(35.3%)	23(45.1%)	0.421
Baseline serum creatinine, µmol/l (mean± SD)	169.3 ± 48.3	157.1±36	181.5±55.7	0.01
creatinine clearance, ml/min (mean± SD)	35.7±10.6	37.2±10.8	34.2±10.2	0.147
Chronic kidney disease, n (%)	98(96.1%)	48(94.2%)	50(98%)	0.351
Hemoglobin, g/dl (mean± SD)	11.5±1.9	11.6±2	11.2±1.7	0.269
Hematocrit, % (mean± SD)	35±5.4	35.5±6	34.6±4.9	0.366
Anemia, n (%)	63(61.8%)	32(62.7%)	31(60.8%)	0.839
Glycaemia, mmol/l, (mean± SD)	8.9±3.3	8.9±3.3	9±3.4	0.864
Mehran score	9.6 ± 2.5	9.2 ± 2.4	9.9 ± 2.6	0.168
Moderate risk	71,6%	76,5%	66,7%	0,53
High risk	26,5%	21,6%	31,4%	0,53
Very high risk	1,9%	1,9%	1,9%	0,53

LV EF : Left ventricular ejection fraction, SD : standard deviation

Procedural Characteristics

The types of procedures performed in both groups were comparable.

On average 57.8 ± 33.4 ml of contrast were used corresponding to 0.78 ± 0.47 ml / kg. A trend towards greater contrast volume was observed for the Iopromide group compared to the Iodixanol group (63.6 ± 36.7 vs. 51.2 ± 2.9ml, p = 0.077) corresponding to (0.87 ± 0.52 vs.0.69 ± 0.4ml / kg; p = 0.051) [Table 2].

Table 2: Procedural characteristics of the study population

Type of procedure, n (%)	Study population	Group U (N=51)	Group V (N=51)	p
Coronarography alone	65 (63.7)	31 (60.8)	34 (66.7)	NS
Elective angioplasty	22 (21.6)	12 (23.5)	10 (19.6)	NS
Ad hoc angioplasty	15 (14.7)	8 (15.7)	7 (13.7)	NS
Contrast volume, ml (mean± SD)	57.8 ± 33.4	63.6 ± 36.7	51.9 ± 29	0.077
Contrast par kg, ml/kg (mean± SD)	0.78 ± 0.47	0.87 ± 0.52	0.69 ± 0.4	0.051
Contrast according to the type of procedure ml (mean± SD)				
Coronarography alone	47 ± 23.2	53.5 ± 27.9	41 ± 16.2	0.028
Elective angioplasty	75.9 ± 38.8	81.7 ± 40.9	69 ± 37	0.857
Ad hoc angioplasty	78 ± 42.9	75.6 ± 49.9	80.7 ± 37	0.625
Contrast per kg by type of procedure, ml/kg (mean± SD)				
Coronarography alone	0.64 ± 0.32	0.74 ± 0.39	0.54 ± 0.2	0.011
Elective angioplasty	1.01 ± 0.54	1.11 ± 0.58	0.9 ± 0.51	0.559
Ad hoc angioplasty	1.05 ± 0.66	1.02 ± 0.77	1.09 ± 0.57	0.864

Change in serum creatinine and Incidence of CIN

Change in serum creatinine: The serum creatinine and clearance values were stable after coronarography and angioplasty procedures (Δ créatinémie -2.5 mmol/l [-16.5; +18], Δ clairance +0.9 ml/min [-3;+4.1]). There were no significant differences between the Iopromide group and the Iodixanol group (all p >0.05) [Table 3]. The changes in serum creatinine and clearance values were similar according to the diagnostic and therapeutic procedures (p = 0.64 and p = 0.71, respectively).

Incidence and evolution of CIN: Nine patients presented a CIN with an incidence of 8.8%. There was no significant difference between the Iopromide and the Iodixanol group (7.8 vs. 9.8%, p = 0.727). Six cases of CIN occurred following coronary angiography, the remaining 3 cases were observed following angioplasty. The type of procedure (coronarography versus angioplasty) had no impact on the incidence of CIN in both groups (all p> 0.05). In the case of CIN, prolonged hospitalization was noted (4.2 ± 2.1 vs. 1.7 ± 0.8 days, p = 0.02). A decrease in serum creatinine with return to baseline was noted in

Table 3: Changes in serum creatinine and its clearance in the study population

	Study population (N=102)	Group U (N=51)	Group V (N=51)	p
Δ serum creatinine, µmol/l, median [IIQ]	-2.5 [-16.5;+18]	-3 [-13;+15]	-2 [-19;+18]	0.259
Δ serum creatinine according to the type of procedure, µmol/l, median [IIQ]				
Coronarography alone	+3 [-15.5;+18]	+2 [-11;+18]	+4 [-18.5;+18.7]	0.350
Elective angioplasty	-5 [-13;+13]	-4.5 [-12.75;+22.75]	-6 [-16.5;+7.6]	0.438
Ad hoc angioplasty	-7 [-24;+15]	-6.5 [-23.2;+9]	-7 [-37;+23]	0.906
Δ serumcreatinine, %, median [IIQ]	-1.61 [-10.29;+10.4]	-2.29 [-9.13;+10.06]	-0.97 [-11.81;+11.5]	0.387
Δ serum creatinine according to the type of procedure, %, median [IIQ]				
Coronarography alone	+1.59 [-8.77;+10.61]	+1.19 [-11.18;+10.43]	+2.12 [-11.84;+12.12]	0.361
Elective angioplasty	-2.69 [-10.4;+11.5]	-2.46 [-10.87;+13.7]	-3.33 [-8.79;+3]	0.495
Ad hoc angioplasty	-4.32 [-15.67;+8.68]	-4.17 [-14.86;+5.92]	-4.32 [-18.97;+16.67]	0.540
Δ clearance, ml/min, median [IIQ]	+0.9 [-3;+4.1]	+0.85 [-3;+4]	+1 [-3;+5]	0.296
Δ clearance according to the type of procedure, ml/min, median [IIQ]				
Coronarography alone	+0.85 [-3.1;+4]	+0.85 [-4;+3]	+0.8 [-3.1;+5]	0.397
Elective angioplasty	+0.3 [-3.3;+4]	+0.3 [-3.77;+6]	+0.5 [-2.75;+3.95]	0.773
Ad hoc angioplasty	+2 [-3;+5]	+1.5 [-2.25;+7.75]	+2 [-12;+5]	0.220
Δ Clearance, %, median [IIQ]	+2.2 [-10;+14.9]	+2.17 [-8.57;+12.73]	+2.17 [-11.11;+16.67]	0.344
Δ clearance according to the type of procedure, %, median [IIQ]				
Coronarography alone	+2.17 [-10.55;+14.97]	+2.17 [-8.57;+8]	+1.89 [-13.75;+16.91]	0.337
Elective angioplasty	+0.97 [-11.09;+13.03]	+0.97 [-12.45;+13.64]	+0.56 [-7.12;+15.05]	0.785
Ad hoc angioplasty	+ 5.71 [-8.33;+18.18]	+4.05 [-6.25;+17.88]	+5.71 [-23.07;+25]	0.501

5 patients; whereas a stabilization of the creatinine was observed in the 4 remaining patients. No cases of death or dialysis were reported at 3 months in patients with CIN. This evolution was similar in both groups.

Risk Factors for CIN

- Univariate analysis identified the following risk factors for CIN (p<0, 2):
• Baseline serum creatinine> 164µmol / l, p=0,1
• Initial clearance <30ml / min; p=0.17
• Older age (>75 years; P=0.118)
• Administration of large volumes of CM (>1 ml/kg; p=0.145)
The type of contrast medium had no impact on the incidence of CIN (Iopromide vs. Iodixanol, p = 0.728).
- In multivariate analysis, only baseline creatinine> 164µmol / l independently predicted the occurrence of CIN (OR: 10.14, 95% CI 1.22-84.43, p = 0.032).

DISCUSSION

Our study revealed that CIN was infrequent (8,8%) in patients at high risk for CIN (Mehran score>6), undergoing cardiac catheterisation with rigorous hydration. We found no significant difference in its occurrence between those receiving the low-osmolar, non-ionic monomer iopromide 370 and those receiving the iso-osmolar dimer iodixanol 320 (7.8 vs. 9.8%, p = 0.727).
The results of the comparison of iso-osmolar contrast media (IOCM) to low osmolar contrast media (LOCM) have been inconclusive to date; there are contradicting reports on outcomes.
The NEPHRIC study [10], was the first randomized trial to compare the use of a low-osmolar contrast agent with an iso-osmolar contrast agent in high-risk diabetic patients. This study reported that Iodixanol is less likely to result in CIN than iohexol. The incidence of nephropathy using a cutpoint of an increase in the serum creatinine concentration of >=0.5 mg/dL was 3% in the iodixanol arm (2/64) and 26% in the iohexol arm (17/65, p=0.002).
In a randomized study including 208 patients with renal impairment (clearance ≤60ml / min), Nie et al. [12] compared the renal tolerance of Iodixanol (n = 106) versus Iopromide (n = 102) after coronary angiography and or PCI. The incidence of CIN was significantly lower in the Iodixanol arm (5.7% vs. 16.7%, p = 0.011). The predictive factors of CIN were as follows: creatinine baseline (OR 2.21, 95% CI: 1.25-3.47, p = 0.031), Iopromide use (OR 2.56, 95% CI: 1.18- 5.76, p = 0.024), and the volume of CM administered (OR 2.01, 95% CI: 1.01-3.21, p = 0.038) [(72)]. In addition, fewer cardiovascular events were observed in the Iodixanol arm (1.9% vs. 8.8%, p = 0.025).
However, subsequent trials have failed to show a difference in the development of CIN between Iodixanol and Iopromide in patients with preexisting renal dysfunction.
Juergens et al [13] conducted a randomized, double-blind, multicentre study of 191 patients with impaired renal function undergoing a coronary interventional procedure. Primary end-point was the incidence of CIN on day 2, defined as an increase in serum creatinine concentration of 44 µmol/L (0.5 mg/dL) or by a relative increase of 25% from baseline. Secondary end-points included peak increase in serum creatinine between baseline and day 7.
Iodixanol was not associated with a statistically significant lower incidence of CIN when compared with iopromide (23% vs. 27%; p=0.48)
Compared to our study, these rates of CIN are relatively high. This may be due to larger CM volumes used in the study of Juergens et al and to late CIN case detection discovered after the first 48h on the second biological control.
In a population of unselected patients with ST-segment elevation acute myocardial infarction, who underwent primary percutaneous coronary intervention, Bolognese et al [14] reported in the CONTRAST-AMI trial that iopromide was not inferior to iodixanol in the occurrence of CIN. In addition, no significant differences were found in terms of tissue-level reperfusion and major adverse cardiac events between the 2 contrast agents.
Similarly, Shin et al [15]. found no significant difference in the incidence of CIN between these 2 CM used in 450 patients with coronary angiography (Iodixanol vs. Iopromide 10.7% and 7.8%, respectively, absolute difference 2.9%, 95% CI -3.1% to 8.9 %, p = 0.394).
Table 4 summarizes data from various randomized trials comparing the renal safety of Iopromide and Iodixanol.
The main finding of the meta-analysis of Zhang et al [19] was that in the population of patients with renal insufficiency undergoing coronary angiography with or without PCI, the iso-osmolar, nonionic dimer iodixanol was not associated with a significant lower risk in the incidence of CIN when compared with the low-osmolar, nonionic monomeric iopromide.
These findings for the incidence of CIN between iodixanol and iopromide are consistent with other meta-analyses performed by Reed et al, [20] Heinrich et al,[21] and From et al [22].
These three studies drew a similar conclusion that no significant difference in the risk of CIN could be found between iodixanol and LOCM other than iohexol, of which iopromide was included. However, these results seem to conflict with a much earlier meta-analysis by McCullough et al, [23] both in the outcome of CIN and the maximum increase in Cr. In that study iodixanol was demonstrated to had a lower risk for CIN than LOCM among patients with CKD, and the maximum increase in Cr was significantly less in patients treated with iodixanol than with LOCM, both in all patients (P<.001)

and in patients with CKD (P=.004). Each of the meta-analyses mentioned above had subgroup analysis comparing iodixanol to iopromide.

The main limitation of our study was the early timing of the Cr measurements. It might have resulted in an underestimation of the incidence of CIN in both experimental groups. Although the maximum increase in Cr indicative of CIN is generally observed up to 3 days after administration of CM [24] or even 3 to 5 days after CM administration [25], the majority of Cr measurements were available only for day 1 or day 2, and some cases of CIN might have been missed. However, it is unlikely that serious cases of CIN were missed, because they are usually detected within the first 24 h after the contrast exposure [26].

CONCLUSION

In summary, our trial shows that CIN was infrequent in patients at high risk for CIN (Mehran score>6), undergoing cardiac catheterization after rigorous hydration. The use of iodixanol was not associated with a statistically significant lower incidence of CIN when compared with iopromide.

Table 4: literature review of comparaison between Iodixanol and iopromide

	Total patients, N	Renal inclusion criteria	CIN definition	CIN time frame, d	Creatinine assessment, days	Hydration (0,9% saline)	NAC use (%)	CIN Iopromide vs Iodixanol	p
Nie et al, 2008 [12]	208	Cr Cl≤60 ml/mn	Scr↗≥0,5 mg/dl or≥25%	3	2, 3, 5, 6, 7	1000ml	0	16.7% vs 5.7%	0,011
Juergens et al, 2009 [13]	191	Scr>130 µmol/l or Cr Cl≤60 ml/mn	Scr↗≥0,5 mg/dl or≥25%	2	2,7	1200 ml	100	15% vs 12 %(day 2)	0.56
Han et al, 2010 [16]	1708	30≤Cr Cl≤60 ml/mn	Scr↗≥0,5 mg/dl or≥25%	3	3	NA	0	23%vs 27% (day 2 and 7)	<0,001
Shin et al, 2011	420	Cr Cl≤60 ml/mn	Scr↗≥0,5 mg/dl or≥25%	2	1, 2	1ml/kg/h, ≥16h	60	26,3% vs 3,2%	0.394
Bolognese et al, 2012 [14]	133	Cr Cl≤60 ml/mn, STEMI	Scr↗≥0,5 mg/dl or≥25%	3	1, 2, 3, atdischarge	1ml/kg/h 12h	100	7.8% vs 10.7%	NS
Chen et al 2012 [17]	562	30≤eGFR≤60 ml/mn/1,73 m2	Scr↗≥25%	3	72±12 (h), 7	1500 ml	0	10% vs 13%	Non inferiority of iopromide to iodixanol (p<0,001)
Said et al [18] 2013	220	eGFR≤60 ml/mn/1,73 m2	Scr↗≥50%	3	1, 3	Volume unknown	0	0,4% vs 0,3%	
Our study 2016		Mehran score ≥6	Scr↗≥0,5 mg/dl or≥25%	2	2	1 to 1.5ml / kg 12 before and 24 h later		7.8% vs9.8%	0,72

REFERENCES

1. Heinrich MC, Ha¨berle L, Mu¨ller V, Bautz W, Uder M. Nephrotoxicity of iso-osmolariodixanol compared with nonionic low osmolar contrast media: meta-analysis of randomized controlled trials. Radiology. 2009;250(1):68-86.
2. K. Nash, A. Hafeez, and S. Hou, "Hospital-acquired renal insufficiency," American Journal of Kidney Diseases, vol. 39, no. 5, pp. 930–936, 2002.
3. . McCullough PA, Wolyn R, Rocher LL, Levin RN, O'Neill WW. Acute renal failure after coronary intervention: incidence, risk factors and relationship to mortality. Am J Med. 1997;103:368e375.
4. Rihal CS, Textor SC, Grill DE, et al. Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. Circulation. 2002;105:2259e2264.
5. 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 CollCardiol. 2004;44:1393e1399.
6. U. Nyman, J. Bj¨ork, P. Aspelin, and G. Marenzi, "Contrast medium dose-to-GFR ratio: a measure of systemic exposure to predict contrast-induced nephropathy after percutaneous coronary intervention," ActaRadiologica,

vol. 49,no. 6, pp. 658– 667, 2008.
7. C. Mueller, G. Buerkle, H. J. Buettner et al., "Prevention of contrast media-associated nephropathy: randomized comparison of 2 hydration regimens in 1620 patients undergoing coronary angioplasty," Archives of Internal Medicine, vol. 162, no. 3, pp. 329–336, 2002.
8. G. Marenzi, E. Assanelli, I. Marana et al., "N-acetylcysteine and contrast-induced nephropathy in primary angioplasty," The New England Journal of Medicine, vol. 354, no. 26, pp. 2773– 2782, 2006.
9. B. J. Barrett and E. J. Carlisle, "Metaanalysis of the relative nephrotoxicity of high- and low-osmolality iodinated contrast media," Radiology, vol. 188, no. 1, pp. 171–178, 1993.
10.. Aspelin P, Aubry P, Fransson SG et al: Nephrotoxic effects in high-risk patients undergoing angiography. N Engl J Med, 2003; 348: 491–99
11. Jo SH, Youn TJ, Koo BK, Park JS, Kang HJ, Cho YS, Chung WY, Joo GW, Chae IH, Choi DJ, et al. Renal toxicity evaluation and comparison between visipaque (iodixanol) and hexabrix (ioxaglate) in patients with renal insufficiency undergoing coronary angiography: The RECOVER study: A randomized controlled trial. J Am CollCardiol 2006;48:924–930.
12. Nie B, Cheng WJ, Li YF, Cao Z, Yang Q, Zhao YX et al. A prospective, double-blind, randomized, controlled trial on the efficacy and cardiorenal safety of iodixanol vs. Iopromide in patients with chronic kidney disease undergoing coronary angiography with or without percutaneous coronary intervention. CatheterCardiovascInterv. 2008 Dec 1;72(7):958-65
13. Juergens CP1, Winter JP, Nguyen-Do P, Lo S, French JK, Hallani H, Fernandes C et al. Nephrotoxic effects of iodixanol and iopromide in patients with abnormal renal function receiving N-acetylcysteine and hydration before coronary angiography and intervention: a randomized trial. Intern Med J. 2009 Jan;39(1):25-31.
14. Bolognese L1, Falsini G, Schwenke C, Grotti S, Limbruno U, Liistro F et al. Impact of iso-osmolar versus low-osmolar contrast agents on contrast-induced nephropathy and tissue reperfusion in unselected patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention (from the Contrast Media and Nephrotoxicity Following Primary Angioplasty for Acute Myocardial Infarction [CONTRAST-AMI] Trial). Am J Cardiol. 2012 Jan 1;109(1):67-74
15. Shin DH, Choi DJ, Youn TJ, Yoon CH, Suh JW, Kim KI e al. Comparison of contrast-induced nephrotoxicity of iodixanol and iopromide in patients with renal insufficiency undergoing coronary angiography. Am J Cardiol. 2011 Jul 15;108(2):189-94.
16. Han Y,Wang S, Wang X, et al. Contrast-induced nephropathy following coronary intervention in elderly, renally impaired patients: a randomised comparison of the renal safety of iodixanol and iopromide. Euro- Intervention 2010;6.
17. Chen Y1, Hu S, Liu Y, Zhao R, Wang L, Fu G et al. Renal tolerability of iopromide and iodixanol in 562 renally impaired patients undergoing cardiaccatheterisation: the DIRECT study. EuroIntervention. 2012 Nov 22;8(7):830-8.
18. Said K, Elgabail E, Adel A, et al. Contrast-induced acute kidney injury in patients with chronic kidney disease undergoing coronary catheterization: a comparative randomized study between iodixanol versus iopromide contrast media. EurHeart J 2013;34:5490–15490.
19. Zhang J, Jiang Y, Rui Q, Chen M, Zhang N, Yang H et al. Iodixanol versus iopromide in patients with renal insufficiency undergoing coronary angiographywith or without PCI. Medicine (Baltimore). 2018 May;97(18):e0617.
20. Reed M, Meier P, Tamhane UU, et al. The relative renal safety of iodixanol compared with low-osmolar contrast media: ameta-analysis of randomized controlled trials. JACC CardiovascInterv 2009;2:645–54.
21. Heinrich MC, HaberleL,Muller V, et al. Nephrotoxicity of iso-osmolariodixanol compared with nonionic low-osmolar contrast media: metaanalysis of randomized controlled trials. Radiology 2009;250:68–86.
22. From AM, Al Badarin FJ, McDonald FS, et al. Iodixanol versus lowosmolar contrast media for prevention of contrast induced nephropathy: meta-analysis of randomized, controlled trials. CircCardiovascInterv 2010;3:351–8.
23. McCullough PA, Bertrand ME, Brinker JA, et al. A meta-analysis of the renal safety of isosmolariodixanol compared with low-osmolar contrast media. J Am CollCardiol 2006;48:692–9.
24. Morcos SK. Contrast media-induced nephrotoxicity—questions and answers. Br J Radiol 1998;71:357–65.
25. Gami AS, Garovic VD. Contrast nephropathy after coronary angiography. Mayo Clin Proc 2004;79:211–9. 47.
26. Guitterez NV, Diaz A, Timmis GC, O'Neill WW, Stevens MA, Sandberg KR, et al. Determinants of serum creatinine trajectory in acute contrast nephropathy. J IntervCardiol 2002;15:349–54.