Original paper

Zero-contrast percutaneous coronary interventions to preserve kidney function in patients with severe renal impairment and hemodialysis subjects

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Abstract

Introduction: Zero-contrast percutaneous coronary intervention (zero-PCI) is a new method for prevention of contrast-induced acute kidney injury (AKI) in patients with chronic kidney disease (CKD). However, evidence for its feasibility, safety and clinical utility is limited to reports of single cases or series of patients.

Aim: To present outcomes of zero-PCI in patients with severe CKD, including hemodialysis subjects, who were treated with this procedure in order to preserve their renal function.

Material and methods: Twenty-nine zero-PCIs were performed, mostly as a staged procedure, in 20 patients with advanced CKD. In this group, 4 patients were treated with hemodialysis but presented preserved residual renal function. The estimated median risk for contrast-induced AKI in non-dialysis patients was 26% (26–57%).

Results: Zero-PCI was feasible in each intended patient, including those with complex left main stenosis or lesion within a saphenous vein graft, and there was no specific complication associated with this technique. After the procedure, the factual AKI prevalence was 10% and no patient required renal replacement therapy. Three of 4 hemodialysis patients preserved their residual renal function. During the median follow-up of 3.2 (1.2–5.3) months no patient experienced an acute coronary event or required revascularization.

Conclusions: Zero-PCI is a safe and promising method to preserve renal function in patients with CKD and hemodialysis patients. Such an approach is feasible even in complex coronary lesions and yields good clinical outcomes in mid-term observation.

Key words: renal insufficiency, contrast-induced nephropathy, acute kidney injury, zero-contrast percutaneous coronary intervention.

Summary

Zero-contrast percutaneous coronary intervention (zero-PCI) is a new strategy for prevention of contrast-induced acute kidney injury (AKI). This study presents outcomes of 29 zero-PCIs performed in 20 patients with severe chronic kidney disease. Zero-PCI was feasible in each intended patient and there was no specific complication associated with this technique. The estimated median risk of AKI of 26% (26–57%) before zero-PCI dropped to the observed prevalence of 10%, and during the median follow-up of 3.2 (1.2–5.3) months no patient experienced an acute coronary event or required revascularization.

Introduction

Contrast-induced acute kidney injury (AKI) is a severe complication of percutaneous coronary intervention (PCI) in patients with chronic kidney disease (CKD) and is responsible for various adverse outcomes such as deterioration of renal function, necessity of dialysis, prolonged hospitalization and increased mortality [1, 2]. The risk of AKI is particularly high in CKD patients with multiple comorbidities including diabetes mellitus, congestive heart failure, hemodynamic instability, reduced plasma volume and anemia [3, 4]. Since the incidence of AKI increases almost linearly with the amount of contrast, every method allowing contrast volume reduction

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may protect renal function [2, 3]. Zero-contrast PCI (zero-PCI) is a new emerging method for the prevention of AKI among patients with CKD [5]. However, despite initial promising results, experiences in this approach are still limited to single cases or series of patients [5–14]. Moreover, it is not known if such an approach plays any positive role in preserving residual renal function in hemodialysis patients. Since the procedure without contrast administration is demanding and may be associated with some potential complications, more evidence for its feasibility, safety and clinical utility is needed before it will be accepted as a daily practice by a wide interventional community.

Aim

The aim of this retrospective analysis was to present outcomes of zero-PCI in patients with severe CKD, including hemodialysis subjects, who underwent this procedure in order to preserve their renal function.

Material and methods

Patients with renal failure requiring percutaneous revascularization were treated with zero-PCI if they met one of the following criteria: (i) their estimated glomerular filtration rate (eGFR, by the Modification of Diet in Renal Disease equation) was less than 45 ml/min/1.73 m^2; (ii) they previously experienced contrast-induced AKI; or (iii) they were treated with hemodialysis but presented preserved residual renal function defined as urine output ≥ 500 ml/day [15]. The main exclusion criteria were: ST-segment elevation myocardial infarction (STEMI), shock, chronic total occlusion and terminal chronic renal failure with no residual diuresis. However, patients after recent STEMI who required further revascularization and AKI prevention were also qualified for zero-PCI as a staged procedure. Patients with non-ST-segment elevation myocardial infarction (NSTEMI) were suitable for such an intervention if their infarct-related artery was patent without obvious thrombus on the initial coronary angiography. Previous coronary artery bypass grafting (CABG) and the need for rotational atherectomy in non-tortuous artery were not exclusion criteria. Individual risk of AKI before zero-PCI was estimated according to the Mehran risk score with the assumption that contrast dye is not used [3]. Contrast-induced AKI was defined as an increase in the serum creatinine level of more than 0.5 mg/dl (44 µmol/l) or an increase of at least 25% in the level from baseline within 72 h after the procedure [1].

Stable patients with known significant renal impairment underwent ultra-low contrast coronary angiography where the intended maximum contrast volume was pre-defined as less than or equal to 15 ml – details on how to perform such an examination have been summarized elsewhere [16]. However, unstable patients with acute coronary syndrome usually first underwent standard interventions and then, if they needed further revascularization, zero-PCI was performed as a staged procedure. For zero-PCI, coronary angiography was analyzed in detail and the suitable angiographic images were displayed alongside the active fluoroscopy screen as a reference – the guidewires were inserted according to these reference images. The procedure was guided by intravascular ultrasound (IVUS), i.e. IVUS identified the lesion length, determined balloon and stent diameters, and landing zones for stent implantation, as well as verified and documented the final PCI effect. Landing zones were determined at the first non-diseased vessel segments close to the lesion or at segments with plaque burden less than 50% in cases with diffuse lesions. The reference diameters for selection of balloons and stents were determined by the maximum lumen diameter of the distal landing zone – if another stent had to be proximally placed, the proximal landing zones was a reference. The stent length was based on the distance between the distal and proximal landing zones and was measured with a calibrated Volcano IVUS probe. The PCI result was assessed in IVUS by calculating the stent expansion which corresponded to the ratio of the minimum stent area over the mean of the proximal and distal stent reference lumen areas multiplied by 100% (percentage). A detailed description of the zero-contrast method and its procedural options may be found elsewhere [16]. Due to legal issues, at the end of procedure, a single injection of small contrast volume (usually 5 ml) was performed in each patient to document the angiographic PCI result and lack of complications (e.g. distal perforation or embolization). Other indications for contrast injection during the intervention included: chest pain, persistent drop in blood pressure, new electrocardiographic changes and any suspicion of complications. To become familiar with this technique, operators had to undergo a training program which relied on the guidewire insertion and balloon as well as stent positioning without contrast usage during several standard PCIs (i.e. under ultimate control of contrast injections) and then, for maintenance of the skill, they repeated such a procedure periodically.

All patients provided their informed written consent for the procedure and the treatment strategy was accepted by the institutional review board.

Statistical analysis

Continuous variables were presented as mean ± standard deviation or median and interquartile range where it was appropriate according to normality tests. Categorical variables were presented as numeric values and percentages. Differences in renal function parameters before and after zero-PCI were compared using Student's paired *t*-test or the Wilcoxon signed-rank test. The threshold probability of $p < 0.05$ was taken as the level of statisti-

cal significance. All analyses were performed using NCSS 12 Statistical Software (2018). NCSS, LLC. Kaysville, Utah, USA, ncss.com/software/ncss.

Results

The study group consisted of 20 patients aged 73.7 ±12.8 years with severe renal impairment (eGFR 24.8 ±12.5 ml/min/1.73 m^2) who underwent zero-PCI for prevention of AKI – 4 of these subjects were chronically treated with hemodialysis. Thirteen (65%) patients were admitted due to acute coronary syndromes, i.e. 3 (15%) with STEMI, 6 (30%) with NSTEMI and 4 (20%) with unstable angina. Three (15%) patients were hospitalized because of heart failure, 2 (10%) due to sustained ventricular tachycardia and 2 (10%) were admitted for elective PCI. Table I presents patients' characteristics. Before zero-PCI, ultra-low contrast coronary angiography was performed in 9 patients including hemodialysis subjects (median contrast volume: 13 (11–24) ml). In 2 patients with advanced CKD, who were admitted for elective intervention, coronary angiography was performed during previous hospitalization. However, 9 unstable patients with acute coronary syndrome first underwent standard coronary angiography and PCI of the infarct related artery with median contrast volume of 150 (70–200) ml, and consequently two of them developed contrast-induced AKI requiring temporal hemodialysis – since they all required further revascularization, staged zero-PCI was performed after renal function stabilization.

In general, zero-PCI was performed within 29 coronary arteries in 20 patients with advanced CKD. Sixteen of these subjects underwent staged procedures with a median time of 6 (5–8) days after the first intervention. Multi-vessel zero-PCI was done in 7 cases. One patient with severe calcified lesions was treated with rotational atherectomy but another presenting obstruction within the saphenous vein graft required insertion of a distal protection device – both procedures were done without contrast injection.

After each intervention, due to legal issues, a small amount of contrast dye was injected to confirm the final result and exclude complications (median contrast volume: 5 (3.5–9) ml). Procedural data concerning zero-PCI are presented in Table II.

According to the Mehran risk score, the estimated median risk for contrast-induced AKI before zero-PCI was 26% (26–57%) in non-dialysis patients. The creatinine and eGFR levels did not differ significantly before and after the intervention (mean change: 0.1 ±0.31 mg/dl, p = 0.2; and –0.7 ±10.9 ml/min/1.73 m^2, p = 0.8, respectively). However, in 2 patients the creatinine value slightly exceeded the pre-defined threshold for AKI after zero-PCI; hence the AKI prevalence turns out to be 10%. Importantly, 2 patients who previously developed contrast-induced AKI requiring hemodialysis after standard coronary angiography and PCI did not experience AKI after zero-PCI. In 1 patient, the troponin T value exceeded the level for type 4A myocardial infarction, yet without clinical consequences (IVUS and the final single contrast

Table I. Patients' characteristics

Parameter	Overall group
Clinical characteristics:	
Age [years]	73.7 ±12.8
Males	12 (60)
ACS	13 (65)
Hemodialysis patients	4 (20)
Diabetes mellitus	13 (65)
Hypertension	16 (80)
CHF	16 (80)
VHD	5 (25)
LVEF (%)	42.2 ±12.8
Previous MI	2 (10)
Previous PCI	1 (5)
Previous CABG	3 (15)
Dyslipidemia	7 (35)
Current smoking	1 (5)
Baseline laboratory values:	
Troponin T	202.8 (89.5–995.5)
WBC [× 10^3/µl]	8.1 (7.2–12.2)
RBC [× 10^6/µl]	3.9 ±0.8
Hemoglobin [g/dl]	11.6 ±2.3
HCT (%)	35.9 ±6.7
PLT [× 10^3/µl]	225 (184–257)
Creatinine [mg/dl]	3.2 ±1.9
eGFR [ml/min/1.73 m^2]	24.8 ±12.5
Coronary artery disease:	
One-vessel disease	0 (0)
Two-vessel disease	7 (35)
Three-vessel disease	13 (65)
Left main disease	1 (5)
Bypass graft disease	2 (10)

Values are n (%), mean ± SD or median (Q1–Q3). ACS – acute coronary syndrome, CHF – congestive heart failure, VHD – valvular heart disease, LVEF – left ventricular ejection fraction, MI – myocardial infarction, PCI – percutaneous coronary intervention, CABG – coronary artery bypass graft, WBC – white blood cells, RBC – red blood cells, HCT – hematocrit, PLT – platelets, eGFR – estimated glomerular filtration rate. Coronary artery disease was recognized if the diameter stenosis was at least 50%.

administration did not reveal abnormalities) [17]. In 1 patient with NSTEMI, the final small contrast injection revealed distal embolization which was subsequently treated with anticoagulants and antiplatelet agents. During the median follow-up period of 3.2 (1.2–5.3) months, one woman with severe pulmonary hypertension died after 6 months due to right ventricular heart failure – death not related to the procedure.

Four hemodialysis patients had a median diuresis of 900 (763–1150) ml/day before and 875 (263–1000) ml/day after the intervention (p = 0.8), and 3 of them preserved their residual renal function after zero-PCI. In one of these patients, who underwent a 3-vessel zero-PCI, the renal function improved within some weeks, i.e. the diuresis increased from 800 to 1000 ml/day and the rate of dialyses was reduced from 3 to 2 times per week. Another patient lost the residual renal function within several weeks after hospitalization, i.e. his diuresis dropped from 1000 to 100 ml/day. Table III presents the summary of patients' outcomes and medications.

Table II. Zero-contrast PCI

Procedural data	Overall group
Number of vessels treated with zero-contrast PCI	29
Staged PCI	24 (83)
Time between coronary angiography and staged PCI [days]	6 (5–8)
Left main artery	1 (3)
Left anterior descending artery	11 (38)
Left circumflex artery	10 (34)
Right coronary artery	6 (21)
Saphenous vein graft	1 (3)
Diameter stenosis (%)	85.3 ±8.7
Lesion length [mm]	35.4 ±19.6
Lesion area [mm^2]	2.9 (2.6–3.4)
Lesion plaque burden (%)	76 (70–79)
Minimal stent area [mm^2]	6.5 (5.3–7.6)
Stent expansion (%)	95 (88–103)
Guide wires	2 (1–2)
Number of stents	2 (1–2)
Total stent length [mm]	42.9 ±19.7
Stent diameter [mm]	3 (2.5–3.5)
Pre-dilation	42 (88)
Post-dilation	41 (85)
Rotational atherectomy	1 (5)
Distal embolic protection	1 (5)
Procedure time [min]	69 ±26
Radiation dose [mGy]	1485 ±828
Final contrast injection [ml]	5 (3.5–9)

Values are n (%), mean ± SD or median (Q1–Q3). PCI – percutaneous coronary intervention. Pre-dilation and post-dilation relate to each implanted stent (total number of stents is 48).

Table III. Outcomes of zero-contrast PCI and discharge medications

Variable	Overall group
Hospitalization:	
Change in creatinine [mg/dl]	0.1 ±0.31
Change in eGFR [ml/min/1.73 m^2]	–0.7 ±10.9
AKI after zero-contrast PCI	2 (10)
Renal replacement therapy (non-dialysis patients)	0 (0)
Periprocedural MI	1 (5)
Distal embolization	1 (5)
Follow-up:	
Follow-up period	3.2 (1.2–5.3)
ACS	0 (0)
Stent thrombosis	0 (0)
Repeat revascularization	0 (0)
Stroke	0 (0)
Renal replacement therapy (non-dialysis patients)	0 (0)
Death	1 (5)
Medications:	
Aspirin	20 (100)
Thienopyridine	20 (100)
Anticoagulant	9 (45)
β-Blocker	18 (90)
α-Blocker	11 (55)
ACEI/ARB	9 (45)
Calcium channel blocker	11 (55)
Nitrate	3 (15)
Statin	14 (70)
Diuretic	16 (80)
Oral hypoglycemic agent	5 (25)
Insulin	5 (25)

Values are n (%), mean ± SD or median (Q1–Q3). PCI – percutaneous coronary intervention, eGFR – estimated glomerular filtration rate, AKI – acute kidney injury, MI – myocardial infarction, ACS – acute coronary syndrome, ACEI/ARB – angiotensin-converting enzyme inhibitor/angiotensin receptor blocker.

Discussion

Zero-contrast PCI is a new promising approach in the prevention of AKI in patients with severe CKD. However, current evidence for its feasibility and safety is based on case reports and one retrospective study involving 31 patients [5–14]. Therefore, any new clinical data verifying this method provides valuable information on its effectiveness, which is paramount for its wider dissemination among the interventional community. Until now, zero-contrast techniques were employed only in stable patients, and subjects with acute coronary syndromes were not considered for such interventions [6]. This retrospective analysis summarizes the mid-term outcomes of zero-PCI carried out in a heterogeneous group of patients involving both stable subjects and unstable ones with acute coronary syndromes. The rationale for such an approach was to reduce renal function deterioration in a wide range of high-risk patients, e.g. in individuals with severe CKD who recently underwent standard primary PCI or experienced contrast-induced AKI. The estimated median probability of AKI in non-dialysis patients was 26% according to the Mehran risk score, but this risk was calculated with the assumption that contrast dye was not used – if these patients were treated with standard PCI using 100–200 ml of contrast medium, the median risk would increase to 57%. Thanks to the zero-contrast approach, the factual risk of AKI was reduced to 10% and no patient required renal replacement therapy. Of note, two patients who previously developed contrast-induced AKI after standard coronary angiography and PCI did not experience AKI again after zero-PCI.

There was one periprocedural "laboratory" myocardial infarction, yet without any clinical sequelae [17]. At the end of the procedure, due to legal issues, each patient obtained a small contrast volume (usually 5 ml) to document the final PCI result. Such a small contrast amount should not pose any relevant problem in terms of renal function, but it allowed us to recognize distal embolization in one patient with NSTEMI which was undetectable in IVUS, and consequently an adequate drug therapy was employed. During the median follow-up period of 3.2 (1.2–5.3) months, no patient experienced acute coronary event or required revascularization.

In the study group, there were 4 hemodialysis patients with preserved residual renal function. Three of these patients maintained their renal function, but in one patient the diuresis significantly dropped within some weeks after hospitalization. The latter patient had just started elective hemodialysis during the index hospitalization and other causes beside the coronary intervention might play a role in this loss of function. Namely, an initiation of hemodialysis by itself may suppress diuresis in some patients, which is associated with a number of factors, e.g. type of dialysis, hydration, congestive heart failure, diabetes and medications [18–20]. Therefore, it is unlikely that zero-PCI was the cause of the loss of renal function in this subject. In another hemodialysis patient, who underwent a 3-vessel zero-PCI, the left ventricular function improved along with residual renal function and after some weeks the rate of dialysis was reduced. To the best of our knowledge, there is no report on zero-PCI in patients on chronic hemodialysis, but such an approach may help in preservation of their remaining renal function. Importantly, it has been demonstrated that the residual renal function is a prognostic and independent factor of quality of life, morbidity and survival in dialysis patients, and therefore every protective measure to preserve this function is worth considering [21]. Nevertheless, suitable prospective studies should address this strategy before it is recommended in clinical practice.

Study limitations

Several limitations of this study need to be acknowledged. This is a small and non-randomized study performed in a single center, which involved a heterogeneous group of patients, i.e. both stable and unstable ones, who faced a very high risk of AKI. Some patients were initially treated with standard procedures in the acute phase but zero-PCI was employed during further steps of revascularization as a staged intervention to protect their renal function. Although this makes the data non-homogeneous, it shows that the employment of zero-PCI at any stage of revascularization may bring benefit to patients with severe renal dysfunction. Each zero-PCI was done without contrast usage; nevertheless, at the end of the procedure usually one confirmatory injection of median contrast volume of 5 (3.5–9) ml was performed due to legal issues. Such a small amount of dye should not induce AKI, but this needs to be tested in further experiments. Finely, for more objective assessment of the real clinical benefit of the zero-contrast approach, randomized trials on large groups of patients are necessary. Despite all these limitations, the results of this study show that zero-PCI is feasible and is not associated with any specific complications.

Conclusions

This retrospective analysis shows that zero-contrast PCI is a safe and effective method to preserve renal function in patients with severe renal impairment and hemodialysis subjects. Moreover, it yields good clinical outcomes in mid-term observation. Since the procedure was based on IVUS imaging, it allowed us to optimize stent implantation with good procedural results, and consequently no stent thrombosis occurred during the follow-up. Thanks to the training program, the learning curve for the experienced operators was steep and there was no conversion to standard PCI in the study group. Therefore, if the patient's profile or clinical situation indicates that the risk of AKI is high, zero-PCI should be

considered as a preventative solution – this also refers to dialysis patients with residual renal function.

Conflict of interest

The authors declare no conflict of interest.

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