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Effects of staged versus ad hoc percutaneous coronary interventions on renal function—Is there a benefit to staging?☆,☆☆

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ABSTRACT

Aim: The purpose of this study is to determine whether ad hoc (same session) percutaneous coronary intervention, and staged (multiple session) percutaneous coronary intervention (PCI) have different renal outcomes.
Methods and Results: This is a retrospective cohort study that compares the maximal decline in glomerular filtration rate (GFR) at various times points (3–6 days, 1–4 weeks, 4–12 weeks) after either ad hoc or staged PCI. 115 patients undergoing staged PCI and 115 matched ad hoc PCI controls were included in the study. They were equivalent in baseline GFR, left ventricular ejection fraction and intra-procedural volume status based on LVEDP. The group undergoing staged PCI had greater cumulative fluoroscopy time, SYNTAX score and number of stents placed. Staged PCIs used less contrast per catheterization (155.0 ± 5.6 mL) but higher cumulative contrast dose (326.6 ± 14.0 mL) compared to ad hoc PCIs (193.4 ± 7.2 mL). Following intervention, there was a progressive decline in renal function that did not significantly differ between the ad hoc and staged groups. In the subgroup of patients with initial GFR ≤60 cm^3/min, staged PCI was associated with 2.6-fold greater decline in renal function 4–12 weeks after the procedure compared to ad hoc. A propensity match analysis performed in patients with GFR ≤60 cm^3/min confirmed worse renal function in the staged group at 4–12 weeks.
Conclusions: Staged PCI exposes patients to greater cumulative contrast agent loads. The decline in renal function observed in both groups did not differ significantly, however worse renal outcomes were observed in the staged PCI group with baseline GFR ≤60 cm^3/min.

1. Introduction

Percutaneous coronary interventions (PCIs) may involve treatment of single-vessel or multi-vessel interventions performed in either one or more stages (ad hoc and staged PCIs respectively). The decision to stage a PCI is complex and involves logistical, procedural, angiographic and patient factors. In an analysis of 315,241 PCI procedures in Medicare patients, it was estimated that approximately 3% were staged PCIs [1]. Based on an American College of Cardiology survey of 441 cardiologists performed in 2010 the most common reasons for staging PCIs for the treatment of multi-vessel CAD were poor renal function, contrast dose, lesion complexity and the presence of ACS [2]. However, the supposed nephro-protective effects of staged PCIs compared to ad hoc PCIs have not been rigorously studied.

Contrast-induced nephropathy (CIN), the development of acute kidney injury (AKI) after exposure to radiocontrast material, is thought to be multifactorial and often leads to persistent renal dysfunction [3]. Renal tubular cytotoxic damages from high-osmolar contrast exposure with ischemic tubular injury from glomerular arteriolar vasospasm due to imbalances in vasoactive mediators such as nitric oxide, prostaglandins and adenosine are some of the elements involved in CIN [4–10]. The incidence of CIN following PCI varies widely, but is estimated between 1% and 6% in the general population and over 20% in high risk groups [11,12]. Post-PCI CIN is associated with higher mortality and progression to chronic kidney disease (CKD) [13]. Older age, type

Abbreviations: PCI, percutaneous coronary intervention; CAD, coronary artery disease; CIN, contrast induced nephropathy; AKI, acute kidney injury; CKD, chronic kidney disease; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST-elevated myocardial infarction; CRRT, continuous renal replacement therapy; GFR, glomerular filtration rate; MDRD, Modification of Diet and Renal Disease; LVEDP, left ventricular end diastolic pressure; UA, unstable angina.

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and volume of contrast agent, diabetes, congestive heart failure and underlying CKD are some of the traditional factors associated with an increased risk of developing CIN [14–19]. While staged PCI decreases the amount of radiocontrast per procedure, there is currently no evidence on rates or severity of CIN in staged PCIs compared to ad hoc PCI. The aim of this study was to determine the effect of staged PCI and ad hoc PCI on renal function.

2. Methods

2.1. Study design and patient selection

This investigation was a retrospective matched cohort study that examined renal outcomes of patients undergoing staged and ad hoc PCIs. All patients undergoing staged PCIs (defined as more than one PCI within the span of 30 days on elective basis), from January 2012 and December 2014 at Einstein Medical Center, Philadelphia were evaluated for the study. Patients were excluded for any of the following criteria: ST elevation myocardial infarction, shock, need for mechanical circulatory support devices, major complication after index procedure (death, emergent cardiac surgery, intraprocedural complications including acute and subacute stent thrombosis, CVA or hemodynamically significant access related bleeding), chronic total occlusion of coronary artery, chronic hemodialysis and missing data. Patients on acute or chronic nephrotoxic medications (non-steroidal anti-inflammatory medications, aminoglycosides, calcineurin inhibitors, anti-retrovirals, or amphotericin B, acyclovir, sulfonamides etc.) or who had concurrent radiocontrast agent for other radiologic studies were also excluded.

Ad hoc PCI was defined as single-staged PCI where diagnostic angiography and PCI was performed in the same session. The staged cohort was matched one-to-one with patients who underwent an ad hoc PCI for age, sex and baseline glomerular filtration rate (GFR), during the same time period. Complete revascularization (CR) was defined as revascularization of all significant arteries that threaten viable myocardium with stenoses either >70% diameter narrowing by angiography, or of hemodynamic significance by stress testing or invasive assessment as recommended by the Expert Consensus Statement from the Society for Cardiovascular Angiography and Interventions on Staged PCIs [20]. The assessment for CR in this study was based on the individual angiographer's discretion. This study was approved by the local institutional review board. No extramural funding was used for the completion of this study.

2.2. Clinical data and outcome measures

Demographic, clinical and intra-procedural data were collected from the electronic medical record and cardiac catheterization reports. Baseline and post-procedure GFRs were calculated from serum creatinine values obtained <30 days before the index procedure, 3–6 days, 1–4 weeks and 4–12 weeks after the final PCI respectively, using the Modified Diet in Renal Disease (MDRD) equation. Within these groups, the lowest GFR recorded during each follow-up period was used for calculation.

2.3. Statistical analysis

Demographics, clinical information and PCI characteristics were summarized with descriptive statistics and compared using either Students' *t*-test (continuous variables) or *Z*-test (proportions). Contrast volumes were compared using analysis of variance (ANOVA) with Tukey post-hoc testing. The percent change in GFR was calculated using the formula: $100 * [GFR_X - GFR_{initial}]/GFR_{initial}$. The percent change in GFR stratified by time and PCI type was compared using a two-way ANOVA with Bonferoni post-hoc test. Two-tailed *p*-values <0.05 were considered significant. An *a priori* subgroup analysis of patients in both groups with baseline GFR ≤60 cm^3/min was planned, given that this subgroup was at higher risk for AKI. A confirmatory one-to-one propensity match analysis was performed in patients with GFR ≤60 cm^3/min after matching for variables such as age, sex, baseline comorbidities (hypertension, diabetes, hyperlipidemia, prior coronary artery disease), use of renoprotective methods (intravenous fluids, mucomyst), baseline ejection fraction, SYNTAX score and incomplete revascularization to analyze the difference in GFR at 4–12 weeks. All statistical analyses were performed using GraphPad Prism (GraphPad Software Inc., La Jolla, CA, USA) and SPSS 20.0 (IBM, Armonk, NY, USA).

3. Results

3.1. Patient demographics

A total of 981 cases of PCI qualified for inclusion within the study period. 115 patients undergoing staged PCI at Albert Einstein Medical Center between 2012 and 2014 were identified and matched by age, sex, and initial GFR with 115 control patients undergoing ad hoc PCI during the same time period from the rest of the group. The 115 patients within the staged PCI group underwent 243 procedures. These two groups were equivalent with respect to baseline demographics, left ventricular ejection fraction and pre-existing CAD (Table 1). Hypertension was noted more frequently in the staged PCI cohort (93.0% vs. 84.3%). Patients undergoing staged PCI also had higher rates of diuretic and beta-blocker usage prior to PCI (44.4% vs. 31.3% and 91.3% vs. 72.2% respectively). There was no difference in the rates of vascular risk factors such as smoking and diabetes. Usage of other cardiovascular medications (ACEI/ARB/antiplatelets/statins/warfarin) was comparable between the two groups. There were four cases of NSTEMI or UA among the patients who returned for repeat PCI within the staged group. The baseline GFR of the ad hoc and staged PCI groups was 62.3 cm^3/min and 66.6 cm^3/min with 48 (41.7%) and 57 (49.5%) patients having a GFR ≤60 cm^3/min respectively.

Table 1
Baseline characteristics of the study cohort.

Patient characteristics	Ad hoc PCI ($n = 115$)	Staged PCI ($n = 115$)	*p*-Value
Age (mean ± SEM)	74.85 ± 0.90	74.75 ± 0.93	0.936
Sex (%)			
Male	51.2	52.2	0.880
Female	47.8	47.8	1.000
Race (%)			
Caucasian	43.5	48.7	0.430
African American	42.6	35.6	0.275
Other	13.9	15.7	0.704
Cardiac History (%)			
Established CAD	54.8	65.2	0.107
Prior PCI	41.7	51.3	0.144
Prior CABG	24.3	28.7	0.447
Ejection Fraction (mean ± SEM)	49.98 ± 1.15	47.73 ± 1.13	0.924
Comorbidities (%)			
Hypertension	84.3	93.0	0.040
Hyperlipidemia	69.6	62.6	0.262
Diabetes Mellitus	47.8	54.8	0.289
COPD	10.4	12.2	0.667
Tobacco abuse	38.2	43.5	0.412
BMI (mean ± SEM)	28.55 ± 0.57	29.66 ± 0.60	0.524
Medications (%)			
Aspirin	100.0	100	1.000
Clopidogrel	78.2	85.2	0.171
Prasugrel	13.0	10.4	0.542
Ticagrelor	7.0	4.3	0.373
ACEi/ARB	58.2	68.7	0.100
β-Blocker	72.2	91.3	0.018
Diuretics	31.3	44.4	0.040
Statin	80.4	88.7	0.081
Warfarin	2.6	0.9	0.327

SEM: standard error of mean, COPD: chronic obstructive pulmonary disease, ACEi: angiotensin convertase enzyme inhibitor, ARB: angiotensin receptor blocker.