Long-Term Outcomes of Percutaneous Coronary Intervention (PCI) in Octogenarians with Chronic Kidney Disease

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Citation

D Bhatt, F Saeed, M Saqlain, S Arora, V Vanar, M Gibb, J Holley, S Mehta, P Kansara. *Long-Term Outcomes of Percutaneous Coronary Intervention (PCI) in Octogenarians with Chronic Kidney Disease*. The Internet Journal of Cardiology. 2012 Volume 10 Number 2.

Abstract

Background: Few studies have examined the long-term outcomes of percutaneous coronary intervention (PCI) in octogenarians (>80 years old) with chronic kidney disease (CKD). The aim of this study was to evaluate the long-term outcomes of octogenarians with CKD (eGFR < 60mL/min/1.73m2) undergoing PCI in our hospital. Methods: Retrospective data was collected for 319 consecutive patients who underwent PCI during January 2003 to December 2009. Patients were stratified on the presence of CKD (n=143) or no CKD (n=176) as defined by estimated GFR using the MDRD equation and followed for a mean of 33 months. The CKD group had higher rates of diabetes mellitus (40.4% versus 23.4%, p= <0.05), hypertension (98.6% versus 93.8%, p= <0.05), and peripheral vascular disease (19.6% versus 8.5%, p= <0.05). Other characteristics were similar among the groups. The primary outcome of the study was to compare the in-stent restenosis in octogenarians with and without CKD. All cause mortality and bleeding events post stenting were also compared.Results: A total of 59 patients developed in-stent restenosis: 16.6 % (n=29) in non CKD [17.3% with BMS (Bare metal Stents) and 14.3 % with DES (Drug Eluting Stents)] and 21 % (n=30) in the CKD group (22.8% with BMS and 16.7 % with DES) (P=0.31). There was no association of stent type and all cause death in either group; all cause death was significantly higher in the CKD patients. There was no significant difference in bleeding complications in CKD compared with non CKD groups (11.4% versus 10.5%, p= 0.85). However, CKD patients on aspirin and clopidogrel had a significantly higher incidence of bleeding (60% versus 40%, p=<0.001). Conclusion: As previously shown, CKD patients have a higher mortality than those without kidney disease. Long-term outcomes of BMS are comparable to DES in octogenarians with CKD. BMS may be preferable in CKD patients in order to avoid prolonged dual anti-platelet therapy with its attendant higher risk of bleeding in this group.

CKD – Chronic Kidney Disease;
PCI – Percutaneous Coronary Intervention;
CVD – Cardiovascular Diseases;
BMS – Bare Metal Stents;
DES – Drug Eluting Stents;
GFR – Glomerular Filtration Rate;
TVR – Target Vessel Revascularization;
SOB – Shortness of Breath

INTRODUCTION

Octogenarians are a fast growing population in the western world [1]. In the United States, growth is expected in those aged 85 years or above over the next 50 years with approximately 8.5 million Americans in this age group by 2030[2]. This population is expected to have multiple co-morbid conditions like diabetes, previous coronary artery bypass surgery, stroke, and chronic kidney disease (CKD) [3]. In CKD patients, cardiovascular diseases (CVD) are a major cause of morbidity and mortality [4, 5] and CVD is strongly associated with the occurrence and progression of CKD [6]. Octogenarians are increasingly referred for percutaneous coronary interventions (PCI) using either bare metal stents (BMS) or drug eluting stents (DES). Currently, limited data are available on the outcomes of PCI in octogenarian CKD patients. We reviewed our experience with PCI in octogenarians with and without CKD and compared overall mortality, in-stent re-stenosis, and bleeding complications in those treated with BMS and DES.

METHODS

A total of 3,116 patients underwent coronary intervention between January 2003 and December 2009. A retrospective analysis of the 450 octogenarian patients from the 3,116 patients undergoing coronary intervention during the study period was performed. Inclusion criteria were: a) patients ≥ 80 years of age b) PCI was performed on a de-novo coronary artery or coronary artery bypass graft lesion and c) availability of serum creatinine within 30 days of PCI. Three hundred nineteen fulfilled the inclusion criteria and form the study group. The remaining patients were excluded for the following reasons: 110 patients had PCI with stent placement under the age of 80 and PCI was repeated for in-stent restenosis after they were 80 years of age, 2 patients had stent placement for coronary artery dissection, and 19 did not have serum creatinine levels drawn within 30 days of the procedure.

Chronic kidney disease was defined as an estimated glomerular filtration rate (eGFR) below 60ml/min/1.73m^2 for at least a period of three months. eGFR was estimated by the MDRD [7] formula using patient's age, serum creatinine (in mg/dl), race and gender. Patients were divided into two groups based on GFR: those with and without CKD.

Data was collected retrospectively by reviewing electronic medical records for demographic variables and other co-morbidities including hypertension, diabetes, hyperlipidemia, previous bypass surgeries, presence of peripheral vascular disease, the date of stent placement, and the date of in-stent restenosis. The primary end-point of the study was development of in-stent restenosis in each group. Secondary o utcome variables examined were: target vessel revascularization (TVR), recurrent non-fatal myocardial infarction, death, and mean time for development of in-stent restenosis; bleeding complications were also collected for each patient. The cause of death was not analyzed due to unavailability of this information in the medical record for most of the patients. The repeat PCI was performed for 1) worsening of pre-existing angina or shortness of breath 2) new onset angina, 3) recurrent non-fatal MI, or 4) positive stress test for reversible ischemia performed at the end of one year in all patients except patients who presented with any of the above mentioned clinical presentation. Myocardial infarction was defined by EKG criteria for ST segment elevation (STEMI), ST segment depression (Non STEMI), and by cardiac bio-markers. The other co-morbidities were identified by looking for International Classification of Diseases (ICD) codes for diabetes mellitus, hypertension, dyslipidemia, peripheral vascular disease, and previous bypass surgeries. Bleeding was identified by ICD codes gastrointestinal bleeding, intracranial hemorrhage, and nonspecific hemorrhages. Octogenarians who received BMS were given 4-6 weeks of dual antiplatelet therapy (aspirin and clopidogrel). Patients with DES received a minimum of 6 months of dual anti-platelet therapy [8]. The patients were followed for a mean of 33 months.

STATISTICAL ANALYSIS

The patients were stratified into two groups: CKD and non CKD. The data are presented as mean ±SD for continuous variables or as a count (%) for non-continuous variables. Statistical analysis was performed using Chi-square test and independent t-tests where appropriate. Cox-proportional hazards model was performed for development of in-stent restenosis and the factors affecting it. A p value ≤ 0.05 was considered significant.

RESULTS

Baseline clinical characteristics of the groups are shown in Table 1. One hundred forty-three (42.8%) octogenarians had CKD. CKD patients were older and more likely to have diabetes, cancer, and peripheral vascular disease. There was no significant difference between the two groups in site of stent placement, stent size and diameter, and the number of vessels stented. More CKD patients presented with either unstable angina/Non-STEMI or STEMI compared to non-CKD patients. There was no significant difference in the development of in-stent restenosis in CKD and non-CKD octogenarians. The secondary outcomes of PCI between the two groups were also not significant (Table 2). Subgroup analysis based on the type of stent in each group revealed no difference in the development of in-stent restenosis (Table 3). Cox proportionate hazards model showed that CKD patients had a shorter mean time to the development of in-stent restenosis compared to patients without CKD which was not statistically significant (14.56 ±12.8 months versus 16.72 ±12.9 months, respectively, p = <0.76). There was no significant difference in overall bleeding complications among all patients (p=0.55). Twenty-two patients in the non-CKD group and 13 patients in the CKD group were on warfarin, aspirin, and clopidogrel and there was no significant difference in bleeding between these groups. Patients who were on warfarin were given only 81 mg of aspirin. A higher proportion of octogenarians with CKD on long-term aspirin and clopidrogel

Figure 1

Table I. Baseline Clinical Characteristics

Variables	No CKD (n=176)	CKD (n=143)	*p*-value
Age	82.6±2.4	83.4±3.1	<0.05
Male	53.4%	45.5%	0.15
Diabetes	23.4%	40.4%	<0.05
Creatinine	0.97±0.21	1.38±0.46	<0.05
GFR	59.34±2.00	42.92±11.4	<0.05
Hypertension	93.8%	98.6%	<0.05
CVA	26.5%	25.0%	0.79
Dyslipidemia	88.5%	85.0%	0.35
Angina	36.8%	36.2%	0.92
Myocardial Infarction (MI)	49.1%	57.9%	0.12
COPD	17.3%	19.0%	0.70
Cancer	17.9%	28.5%	<0.05
Smoking			0.9
Exsmoker	33.5%	33.3%	
Current smoker	3.9%	3.9%	
Alcohol			0.65
Ex-drinker	4.0%	6.2%	
Current drinker	4.0%	3.1%	
CABG	25.7%	34.3%	0.10
Bare Metal Stents	76.1%	70.6%	0.26
H/O PVD	8.5%	19.6%	<0.05
Death due to all causes	22.0%	45.5%	<0.05

Figure 2

Table II. Outomes of PCI

Variables	No CKD	CKD	*p*-Value
In-stent restenosis	16.6%	21.0%	0.31
Target Vessel Revascularization	9.8%	5.0%	0.11
Recurrent MI	6.3%	11.9%	0.07
Bleeding	11.4%	10.5%	0.55

Figure 3

Table III. Analysis by Group

Variable	No CKD			CKD		
	BMS	DES	*p*-Value	BMS	DES	*p*-Value
In stent re-stenosis	17.3%	14.3 %	0.64	22.8%	16.7%	0.41
Death	23.7%	16.7%	0.376	45.3%	45.5%	0.99

DISCUSSION

There are limited studies assessing outcomes of PCI in octogenarians with CKD. We show there is no significant difference in: 1) in-stent restenosis between CKD and non CKD octogenarians 2) non-fatal MI and TVR after PCI between these two groups, 3) no relationship between the type of stent placed and in-stent restenosis in either the CKD or non-CKD octogenarians, and 4) CKD patients had overall higher mortality. There was no significant difference in bleeding complications between two groups. However, CKD patients who were taking long-term aspirin and clopidogrel were more likely to suffer a bleeding complication.

Chronic kidney disease (CKD) affects a significant percentage of elderly who are the fastest growing segment of the CKD population [9]. CKD is an independent predictor of myocardial infarction (MI), stroke, and all-cause mortality [5]. Practice guidelines from the National Kidney Foundation in 2002 and the American College of Cardiology/American Heart Association Task Force in 2004 recommended that chronic kidney disease be considered a CHD risk equivalent [10]. Moreover, CKD patients also have increased short and long term mortality after an acute coronary syndrome, irrespective of treatment [9]. Thus, increasing attention is and will be devoted to cardiovascular diseases, its diagnosis, treatment, and outcomes among elderly with CKD. The relatively large number of octogenarian patients in our study confirms the frequency of invasive cardiovascular procedures performed in these patients [11] .

Multiple studies have assessed the outcomes of PCI in CKD and non-CKD patients but octogenarians were excluded from most of these studies. In moderate CKD and dialysis patients, a frequent pathological change in blood vessels is plaque calcification along with increased intimal and medial thickness [12]. Yazaki et al conducted a study on 336 patients to assess the effect of paclitaxel eluting stents on intimal thickening and failed to show reduction in cardiac mortality in CKD patients undergoing PCI with paclitaxel eluting stents [13]. Octogenarians are characterized by a high prevalence of coronary artery disease and a growing number of octogenarians are undergoing coronary revascularization. If they have CKD, their overall mortality may be increased [14, 15]. Papafaklis et al enrolled 371 patients (102 with CKD and 269 without CKD) who underwent PCI with either balloon or stent placement. The mean age of patients in the CKD group was 66 years and in the non-CKD group was 58 years. This study showed significantly higher all cause and cardiovascular mortality in CKD patients over a period of 9 years. In this study, adjusted 9-year all-cause and cardiac mortality was increased by approximately 16% and 11%, respectively for a decrease of GFR from 120 to 60 ml/min/ 1.73 m2 and by approximately 14% and 9%, respectively for a decrease of GFR from 60 to 30 ml/min/1.73 m2. The rate of in-stent restenosis between the two groups was not examined.

Previous studies have shown that DES may reduce repeat interventions in octogenarians, but kidney function was not addressed as a distinct variable [16]. DES placement in elderly patients is challenging due to high cost, prolonged duration of dual anti-platelet therapy, and possible increase in bleeding complications. It has been postulated that CKD patients have dysfunctional platelets and are more prone to have higher rates of death, recurrent myocardial infarction, stroke, and bleeding complications [17, 18]. In our study, CKD patients who were on aspirin and clopidogrel had more bleeding complications than those who were not. An observational cross-sectional study conducted by Angiolillo et al.[19] enrolled 306 patients with diabetes with CAD to assess the anti-platelet effect of clopidogrel in CKD patients on dual anti-platelet therapy for at-least 30 days. This study showed that moderate CKD (creatinine clearance 30 to 59 ml/min), and severe CKD (creatinine clearance ≤ 30 ml/min) was associated with a higher degree of platelet reactivity and after adjustment with potential confounders, there was 4-fold increase in platelet reactivity after ADP stimuli and a 2-fold increase in platelet reactivity with collagen stimuli when compared to mild or absent CKD. In addition, these patients had increased markers for platelet activation (p=0.001). The post-hoc analysis of CHARISMA (Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance) trial demonstrated clopidogrel compared with placebo might be harmful in patients with CKD due to diabetes mellitus [18]. In addition, age has been proposed as a potential risk factor development of greater post-treatment platelet reactivity [20, 21] secondary to higher baseline platelet reactivity, altered metabolism related to aging with decrease liver enzymatic function, impaired conversion of clopidogrel to its active metabolite related to aging, and greater prevalence of reduced renal function with aging [22]. Taken collectively, more potent antiplatelet agents may be beneficial in improving cardiovascular outcomes but the benefits may be offset by an increased risk of bleeding complications, particularly in CKD patients who likely have a propensity for bleeding due to abnormal platelet function [23-25].

Our study shows that outcomes of BMS are comparable to DES in octogenarians with CKD. This may be clinically relevant as polypharmacy and medication costs could be reduced by avoiding long term dual anti-platelet therapy in this group of patients by avoiding DES placement. In addition, by avoiding long-term dual anti-platelet therapy we may reduce the risk of bleeding in this subset of patients.

Our findings suggest that BMS implantation is an acceptable option in octogenarians, especially octogenarians with CKD.

STUDY LIMITATIONS

The major limitation is the retrospective nonrandomized nature of the study .Our study was mainly restricted to CKD stage 3 and 4 and included only 4 patients with end stage renal disease. CKD was defined by the MDRD formula which may not accurately reflect kidney function in the extremes of GFR or in the elderly [26]. The study population was small and mainly consisted of Caucasians due to geographic variation.

CONCLUSION

Our study shows that outcomes of BMS are comparable to DES in octogenarians with CKD. This may be clinically relevant as polypharmacy and medication costs could be reduced by avoiding long term dual anti-platelet therapy in this group of patients by avoiding DES placement. In addition, by avoiding long-term dual anti-platelet therapy we may reduce the risk of bleeding in this subset of patients. Our findings suggest that BMS implantation is an acceptable option in octogenarians, especially octogenarians with CKD. Larger studies are required to determine the best treatment options for this patient population.

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