To Compare the Outcomes of Percutaneous Coronary Intervention and Conservative Strategy on Coronary Artery Disease with the Chronic Kidney Disease Patients

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Abstract: *Background: The beneficial effects of revascularization in patients with coronary artery disease (CAD) with chronic kidney disease (CKD) patients remain uncertain, since most often this population were excluded from the studies on revascularization. The aim of the study was to analyze the outcomes between invasive and conservative treatment in this population. Methods: This was a single center, prospective study compared coronary artery disease with chronic kidney disease patients (CAD CKD) with either invasive strategy consisting of coronary angiography and revascularization (if appropriate) added to medical therapy or conservative strategy consisting of medical therapy alone and angiography reserved for those in whom medical therapy had failed. The outcome studied was a composite of death or nonfatal myocardial infarction, non - fatal stroke, re - hospitalization for unstable angina or heart failure, bleeding complication, acute kidney injury requiring dialysis. Results: CAD CKD cohort was predominantly male (85%) with mean age of 60.02 ± 9.95 years. They had higher cardiovascular risk factors like diabetes mellitus (70 %) and hypertension (89 %). The composite outcome of in - hospital death in conservative 3 (4.10%) and invasive 6 (8.9 %) (p=0.2407).7 months follow up mortality, conservative 7 (9.5%) and invasive 3 (4.4%) (p=0.2407). In - hospital heart failure occurred in 13.7% patients in conservative group and in 11.9% in invasive group (p=0.7561). Heart failure at 7 months follow up occurred in 24.6% patients in conservative and 8.9% patients in invasive group respectively (p=0.042). Re - hospitalization occurred in 31.5% in the conservative and 16.4% patients in the invasive groups (p=0.0375). Acute kidney injury requiring dialysis, occurred in 19.2% patients in the conservative and 29.9% patients in the invasive groups (p=0.1412). Non - fatal MI occurred in 9.6% patients in the conservative and 4.5% patients in invasive groups (p=0.2407). Conclusion: In this study there is no evidence that an invasive strategy, as compared with conservative strategy, reduced the risk of death or nonfatal myocardial infarction. However heart failure and rehospitalization events were reduced in invasive group. There was no difference in the bleeding complications and acute kidney injury requiring dialysis in the conservative and invasive groups.*

Keywords: Coronary artery disease (CAD), Chronic kidney disease (CKD), Percutaneous coronary intervention (PCI), Acute coronary syndrome (ACS), Chronic coronary syndrome (CCS)

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death among patients with chronic kidney disease (CKD), 15 - 30 times higher than age - adjusted cardiovascular mortality in the general population. CKD is an independent risk factor for developing coronary heart disease. About 40% of patients with acute coronary syndrome have renal dysfunction and CKD nearly have double mortality in patients with ACS. Patients with CKD are more likely to die from cardiovascular causes than to experience progression to end - stage renal disease requiring dialysis or transplantation[1, 2, 3].

The increased risk and severity of cardiovascular disease in patients with CKD is due to the high prevalence of traditional risk factor such as diabetes, hypertension and dyslipidemia and non - traditional CVD risk factors such as inflammation, oxidative stress, and metabolic bone disease, and vascular calcification play a major role as glomerular filtration rate declines.[2]

Patients with CKD are more likely to have an AMI, rather than chronic stable angina, as their initial clinical manifestation of CAD, and it is more likely to be a non–ST - segment elevation myocardial infarction than an ST - segment elevation myocardial infarction (STEMI) [3]. Reasons may explain why patients with renal dysfunction have poor cardiovascular outcomes after ACS: (a) excess comorbid conditions associated with CKD, in particular, diabetes mellitus and left ventricular dysfunction; (b) therapeutic nihilism; (c) toxicity of therapies; and (d) special biologic and pathophysiologic factors in renal dysfunction that cause worsened outcomes.[4]

The definition and classification of CKD was introduced by the Kidney Disease Improving Global Outcomes in 2004. Chronic kidney disease is defined as abnormalities in kidney damage or glomerular filtration rate <60 mL/min/1.73 m2 that have been present for >3 months[6]. The prevalence of CKD was estimated as 9·1% in the world's population with CKD stages (Table 1), 1–2 accounting for 5·0%, stage 3 for 3·9%,

stage 4 for 0·16%, stage 5 for 0·07%, dialysis for 0·041%, and kidney transplantation for 0·011%. The age - standardised prevalence of CKD was 1·29 times higher in females than in males.[5]

Table 1: Stages of CKD

Progression of CKD by GFR and Albuminuria Categories				Albuminuria categories Description and range		
				A1	**A2**	**A3**
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mol	≥300 mg/g ≥30 mg/mmol
GFR categories (ml/min/1.73m²) Description and range	**G1**	Normal to high	≥90			
	G2	Mildly decreased	60-90			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	15			

Green: low risk (if no other markers of kidney diseases, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk

Patients with CKD are at increased risk for procedural complications, including acute kidney injury (AKI), major bleeding, vessel dissection, MI and death. Observational studies in CKD suggest lower long - term mortality rates in patients with coronary artery disease who were revascularized when compared with patients who did not undergo revascularization, despite an increase in short term. However, these "benefits" may be due to selection biases, compounded by the fact that the medical therapy in these studies was variable and not optimized [2].

For this reason there is risks an unmet need to better understand the optimal management of patients with CAD and CKD [1, 2]. To address these uncertainties, this study has design CAD PCI outcomes in CKD patients to compare with optimal medical therapy (OMT) alone.

2. Materials & Methods

Hospital based, prospective study to compare the outcomes of percutaneous coronary intervention and conservative strategy on coronary artery disease with the chronic kidney disease patients. The study was conducted at the department of cardiology, Government medical college, Thiruvananthapuram, Kerala, India. The patients who are satisfying the inclusion criteria were enrolled in the study. The eligible patients underwent either an initial PCI plus medical therapy when feasible or to an initial conservative strategy of medical therapy alone, with angiography reserved for failure of medical therapy was enrolled in the study.

Inclusion criteria:
Chronic kidney disease and Coronary artery disease both acute coronary syndrome and chronic coronary syndrome after assessing including treadmill stress test and should have undergone percutaneous coronary intervention.

Exclusion criteria:
Coronary artery disease not feasible for PCI, pregnancy, bleeding disorder and contraindication of dual antiplatelet.

3. Results

Baseline characteristics (Table 2): Both groups were comparable in terms of baseline parameters like age, sex and risk factors. The mean age of the population was slightly higher than average coronary artery disease. The difference could be attributed to the atypical presentation in coronary artery disease with chronic kidney disease which can delay seeking medical care and timely diagnosis.

The mean age of the population was 60.19 in the invasive group and 60.4 in the conservative group. In the invasive group 85.1% were males & 14.9% were females & in conservative 86.3% were males and 13.7% were females. This difference was also not statistically significant (p= 0.835) The Age and sex distribution was comparable to that of Ischemia CKD trial which had 80.3% males with average age 62.4 years[1].

Baseline laboratory (Table 3), the mean HB (mean± s. d.) of patients in conservative was 10.9 and in invasive the mean HB (mean± s. d.) 11.2, between the Group was not statistically significant (p=0.2240). The mean EGFR (mean± s. d.) of patients was 29.4 in conservative and in invasive the mean EGFR (mean± s. d.) of patients was 25.9. There was not statistically significant (p=0.0988) between the group.

The echocardiogram (Table 4), in conservative 2 (2.7%) patients had ejection fraction (EF) = 21 - 30 %, 18 (24.7%) patients had EF= 31 - 40 %, 15 (20.5%) patients had EF=41 - 50%, 24 (32.9%) patients had EF=51 - 60 %, 13 (17.8%)

patients had EF = 61 - 70 % and 1 (1.4%) patient had EF ≥71 %.

In invasive, 7 (10.4%) patients had EF= 21 - 30 %, 10 (24.9%) patients had EF=40 %, 17 (25.4%) patients had EF = 41 - 50%, 19 (28.4%) patients had EF= 51 - 60 %, 11 (16.4%) patients had EF=61 - 70 % and 3 (4.5%) patients had EF ≥71 %. Association of ejection fraction between the Group was not statistically significant (p=0.2088).

The Percentage of patients with reduced EF (< 40 %) was lower in the invasive group than conservative group but this difference was not statistically insignificant. CAD CKD cohort was predominantly male (85%) with mean age of 60.02 ± 9.95 years. They had higher cardiovascular risk factors like diabetes mellitus (70 %) and hypertension (89 %).

In - hospital death (Table 5), 3 (4.10%) patients in conservative and 6 (8.9 %) patients in invasive group but not statistically significant (p=0.2407) between the group.10 (13.7%) patients had in - hospital heart Failure in conservative group and 8 (11.9%) patients had in - hospital heart Failure in invasive group with p=0.7561, not significant statistically. In conservative, 7 (9.6%) patients had non - Fatal MI and in - invasive, 3 (4.5%) patients had non - Fatal MI.3 (4.1%) patients in conservative treatment group had stroke. In conservative, 3 (3.0%) patients had Bleeding and 8 (11.0%) patients in invasive, not statistically significant (p=0.1131).

Follow up 7 months (Table 6), 7 (9.5%) patients had mortality in conservative group and 3 (4.4%) patients had mortality in invasive, not statistically significant (p=0.2407) between the group.18 (24.6%) patients had heart Failure and 6 (8.9%) patients had heart Failure both in conservative and invasive group respectively. Association between the group was statistically significant (p=0.042). And re - hospitalization, 23 (31.5%) patients in conservative and 11 (16.4%) patients in invasive had re - hospitalization, which was statistically significant (p=0.0375) between the group.

Table 5: In - hospital events

Events	PCI plus medical therapy Number = %	Medical therapy alone Number =%	P value
Death	6 (8.9%)	3 (4.10%)	0.2407
Heart failure	8 (11.9%)	10 (13.7%)	0.7561
Stroke	0	3 (4.1%)	0.2449
MI	3 (4.5%)	7 (9.6%)	0.207
Bleeding complication	8 (11.0%)	3 (3.0%)	0.113

Table 6: Follow up

Events	PCI plus medical therapy Number = %	Medical therapy alone Number =%	P value
Death	3 (4.4 %0	7 (9.5 %)	0.2407
Heart failure	6 (8.9%0	18 (24.6%)	0.042
Re - hospitalization	11 (16.4%)	23 (31.5%)	0.0375

4. Discussion

The study compared patients of coronary artery disease with chronic kidney disease in two groups. "Invasive" group was patients who were taken up for coronary angiogram with intention of doing a PCI. "Conservative group" include

patients who received guideline directed medical treatment including thrombolysis as per guidelines indication.53 % patients in invasive group and 48 % patients in conservative group has presented with typical anginal pain.

In the invasive group 13 % patients had chest pain of atypical nature or other types of pain compared to 25 % in the conservative group.67 % had anginal equivalent in invasive group and 63 % in conservative group but there is not significant statistically difference between the group so atypical presentation and oligo - symptomatic presentation is common therefore high index of suspicion is critical for diagnosis of coronary artery disease in the chronic kidney disease patients.

Systemic Hypertension was the most common comorbid condition in both groups, closely followed by diabetes and dyslipidemia. The difference between the 2 groups were minor & not statistically significant, 48 % of diabetes mellitus in both groups & P=0.9221; Systemic hypertension, 89.0 % in conservative & 89.6 % in invasive group with p=0.9221. Dyslipidemia, 26 % in conservative group & 10 % in invasive group with p=0.0051 statistically significant between the group.24 % and 18 % were current smoker in conservative and invasive group respectively, no statistically significant between the group, P = 0.438. Family history of coronary artery disease, 6 % each in the both group with the p value = 0.87, not significant statistically. In the Ischemia CKD trial[1], 56 % of the patients had diabetes mellitus, 90 % had hypertension, 11 % were smokers.

In this study (Table 7), stable angina account for 35 (25 %) patients, unstable angina 7 (7.1 %), Non - ST elevation myocardial infarction 52 (37 %) and ST elevation myocardial infarction 46 (32%).

Chronic kidney disease (Table 8), 39 (53.4%) patients had CKD Stage 3, 22 (30.1%) patients had CKD Stage 4 and 12 (16.4%) patients had CKD Stage 5. In Invasive, 33 (49.3%) patients had CKD Stage 3, 14 (20.9%) patients had CKD Stage 4 and 20 (29.9%) patients had CKD Stage 5. Association of Stage of CKD with group was not statistically significant (p=0.1335).

In - hospital mortality and heart failure, statistically not significant between the group and the bleeding complication and acute kidney injury requiring dialysis between the arm was also not statistically significant between conservative therapy and PCI group. The mortality between the group was not statistically significant after 7 months follow up. The overall mortality both in hospital and 7 months follow up was 19 patients (13.5 %). But the heart Failure between the group was statistically significant which was higher in conservative group. The composite heart failure was 42 patients (30%). Non - fatal myocardial infarction and stroke was not statistically significant. Re - Hospitalization was higher in conservative group as compared to PCI group which was statistically significant (p=0.0375). Kaplan - Meier survival analysis for cardiac death was done for all 140 patients in both groups for total duration of 7 months. There was no difference in death between invasive & conservative group (mean 151.20 days vs 151.27 days p =0.84).

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5. Conclusion

The study was a prospective study comparing 2 groups of the patients of coronary artery disease with chronic kidney disease based on the treatment modality they received. The study showed there was no statistically significant difference in death in between the group. Follow up data showed that heart failure was numerically lower in the invasive group (statistically significant). The study showed reduce events of re - hospitalization in invasive group (statistically significant). There is numerically higher incidence of acute kidney injury requiring dialysis and bleeding complication in the invasive group (not statistically significant). The study results conclude that heart failure and re - hospitalization were lower in the invasive group though adverse events like acute kidney injury and bleeding complication were slightly higher than those patients on conservatively managed. Though there was no major difference in in - hospital course the beneficial effects of PCI were significant during follow up with respect to improved patient symptoms and lower hospitalization rate. Findings of the study however necessitate further large - scale RCT to establish the long - term clinical benefit.

6. Study Limitations

1) Sample size of the study was small. A much larger sample size would have given more power to the results & differences between group more significant.
2) Conducting separate study for stable angina and acute coronary syndrome might be more meaningful
3) Details of coronary disease severity was not available for the conservative group
4) Selection bias by the treating Cardiologist for taking up more sicker patients for invasive strategy was not addressed and is an important limitation.
5) A longer follow - up was required to assess the long term outcomes.

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Table 2: Baseline Characteristics

Patients characteristics	PCI plus medical therapy	Medical therapy alone	Total
Total no of patients	68	72	140
Age, mean	60.19	60.4	
Male sex	57	63	120
Family history of coronary artery disease	6	6	12
Current smoking	18	24	42
Hypertension	60	65	125
Hypercholesterolemia	10	26	36
Diabetes mellitus	48	48	96

Table 3: Baseline laboratory

	Invasive Group (n=67)		Conservative Group (N=73)		t	P
	Mean	SD	Mean	SD		
Hb	11.2	1.5	10.9	1.3	1.22	0.2240
TC	10989	2701	10761	2946.8	0.53	0.61
PLC (Lacs)	2.22	0.59	2.29	0.58	0.79	0.43
Urea	29.77	12.27	30.21	16.66	0.2	0.85
Creatinine	3.7212	2.6	3	1.89	1.8	0.062
. eGFR	25.9	13.18	29.42	11.8	1.66	0.098

Table 4: Echocardiography

Echo Parameters	Invasive (n=67)		Conservative (N=73)		t	P
	Mean	sd	mean	sd		
IVS diastole (cm)	1.08	0.16	1.10	0.17	0.77	0.442
IVS systole (cm)	1.71	0.24	1.64	0.24	0.92	0.359
LVID diastole (cm)	4.83	6.9	4.98	6.4	1.24	0.21
LVPW diastole (cm)	1.11	0.19	1.11	0.18	0.25	0.807
LWPW systole (cm)	1.69	0.26	1.61	0.26	0.57	0.572
LA (cm)	3.22	0.47	3.24	0.49	0.36	0.720
Aorta (cm)	3.04	0.45	2.93	0.48	0.94	0.347
EF (%)	49.8	13.1	50.5	11.6	0.75	0.31

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Table 7: Coronary artery disease

Table 8: Chronic kidney disease

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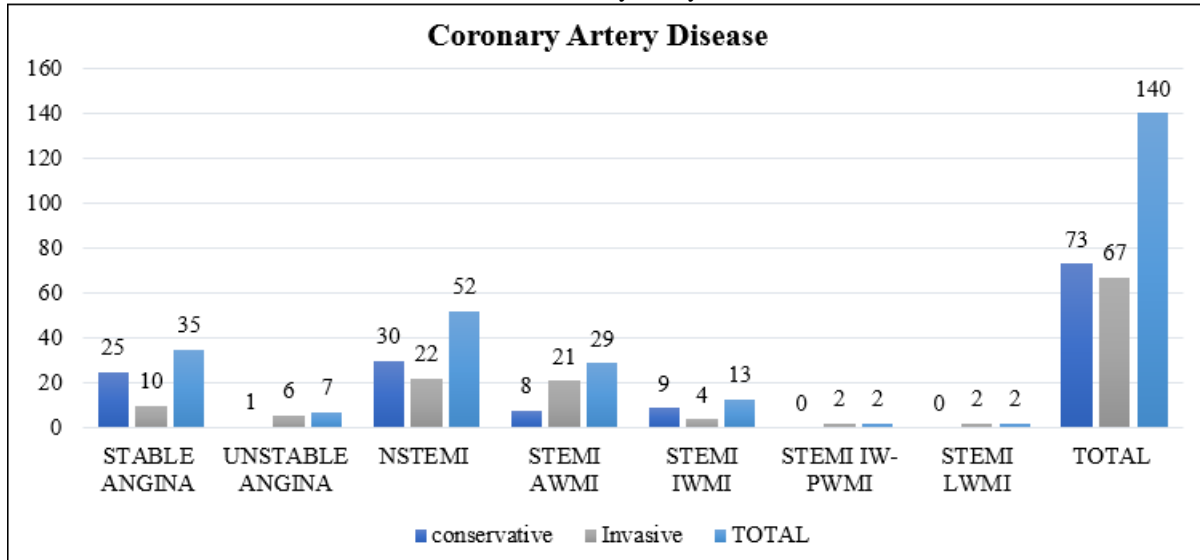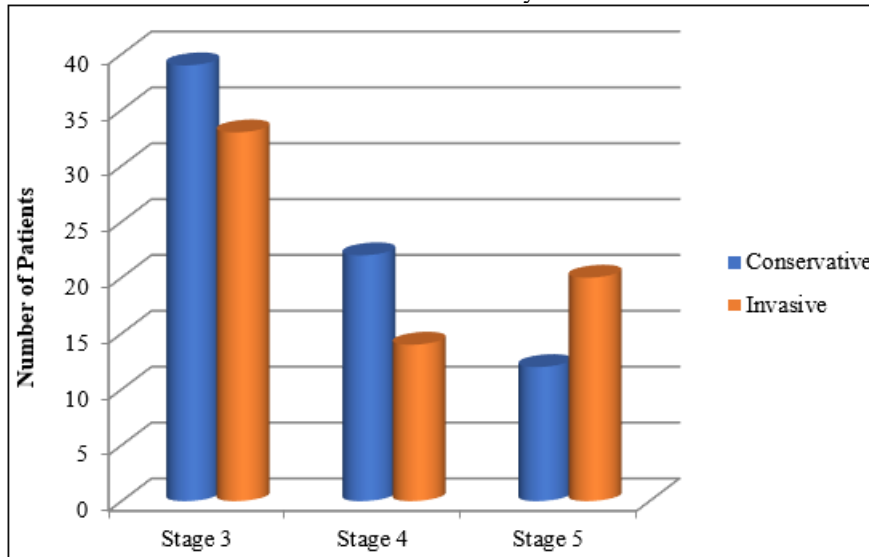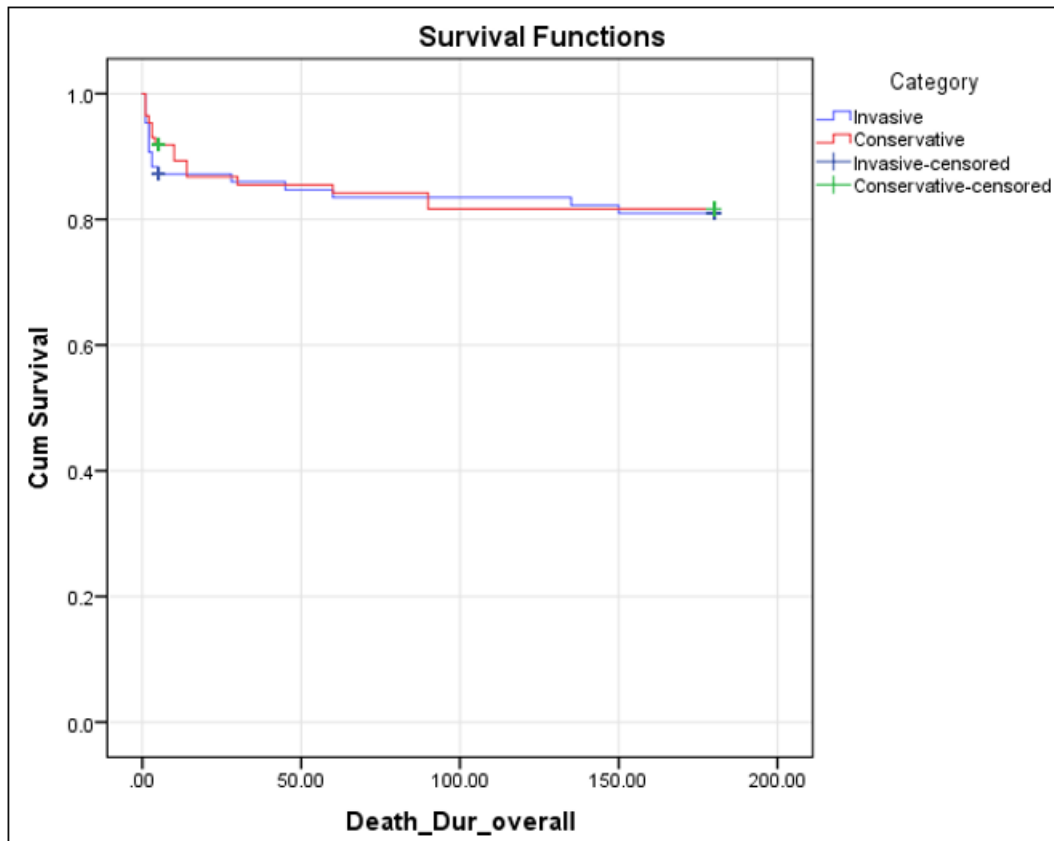
Kaplan Meir overall survival All - cause mortality