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Original Research Article.

Impact of Coronary Revascularization Over Medical Management in Patients of ACS with Renal Dysfunction

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ABSTRACT

Aim: To study impact of coronary revascularization over medical management in patients of ACS with renal dysfunction during hospitalization and follow up.

Method: This study is a case control, single centre study which enrolled 120 patients admitted with diagnosis of ACS with CKD. All patients were divided into two groups on the basis of mode of treatment received, coronary revascularization (PCI or CABG) or optimum medical therapy. Each group was further classified on the basis of renal dysfunction which was defined as creatinine clearance less than 60 ml/min. Crcl 30-60 and Crcl < 30 ml/min were taken as two different categories. All patients were followed upto 1 year for mortality and MACE.

Results: One year mortality was 11.7% in medically managed patients and 1.66% in patients who underwent coronary revascularization. Recurrent angina was common in medically treated group 61.7% patients compared to intervention group 15% (p=0.00001). Other secondary endpoints including stroke, major bleeding, ST elevation myocardial infarction, heart failure occurred more in medically managed group but statistically not significant. Contrast induced nephropathy developed more in revascularization group compared to patients who were managed medically (46.6% V/S 31.8%, p=0.003) but none of them required dialysis.

Conclusion: Coronary revascularization reduced all cause and also significantly reduced in-hospital or follow-up major adverse cardiovascular events without increase in risk of bleeding or need of renal replacement therapy.

Key words: Coronary Revascularization, Myocardial Infarction, Acute Coronary Syndrome, Chronic Kidney Disease, Creatinine.

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INTRODUCTION

Chronic kidney disease (CKD) and acute coronary syndrome (ACS) are highly prevalent diseases and often coexist. The prevalence of CKD dramatically increases with age (4 % at age 20-39 to 47 % at age >70 years).[1] Cardiovascular disease remains the leading cause of morbidity and mortality in these patients. Patients with CKD experience higher rates of bleeding, drug-related adverse events as well as longer hospital stays and increased mortality following coronary revascularization when compared to patients with normal kidney function.[2]

Similarly in patients of acute myocardial infarction (AMI), renal dysfunction was found to be an independent risk factor for mortality.[3] It has been shown that the interaction between the kidney and heart increases the burden for both organs if one becomes diseased. This phenomenon is named cardio-renal syndrome (CRS).[4]

The high prevalence of traditional coronary risk factors such as old age, diabetes, hypertension, dyslipidemia among patients with CKD has been noted previously.[5] Complex interactions like endothelial dysfunction, oxidative stress, smooth muscle proliferation, accelerated atherosclerosis, coronary calcification, left ventricular hypertrophy and decreased coronary perfusion are responsible factors.[6]

In patients who survive an AMI, the presence of CKD is associated with a higher rate of cardiovascular event recurrence and death. Despite it previous studies have reported that these patients are less likely to receive medications, thrombolysis and coronary angiography.[7,8]

Suboptimal management of ACS may be one of the causes of the worse prognosis described in this population. Nevertheless, it is important to mention that even CKD patients receiving optimal

treatment have a poor outcome compared with non-CKD subjects.[3,5] Most trials involving patients with cardiovascular disease have excluded patients with advanced kidney disease.[9,10] Given the greater risk of procedural complications, rapid progression of atherosclerotic disease and high risk of death from nonatherosclerotic causes, treatment guideline for this group of patients remains unclear.

METHOD

This study is a case control, single centre study conducted in SMS Medical College Jaipur between April 2016 to March 2017 and it included 120 patients of ACS with renal dysfunction.

Diagnosis of ACS was based on clinical symptoms, ECG changes or elevated cardiac markers or both according to 2014 ACC/AHA guidelines. Ischemic ECG changes include either transient ST segment elevation or depression > 0.5 mm or persistent and definite T-wave inversion>1 mm including the pseudo-normalization of a previously negative T-wave in two or more contiguous leads.

Patients with chronic stable angina pectoris, those with acute kidney injury and those who refused to given consent were excluded.

CKD is currently defined as kidney damage for atleast 3 months and is characterized by structural or functional abnormalities of the kidneys with or without decreased GFR.[1] All 120 patients with acute coronary syndrome and renal dysfunction were divided into two groups on the basis of mode of treatment coronary revascularization (PCI or CABG) or optimum medical therapy.

Baseline characteristics of all patients were noted, and routine investigation were done. All patients who underwent angiogram were given pre -procedure hydration with i.v normal saline 1-2 ml/kg/hr for 6-12 hr and post procedure hydration with i.v NS 150 ml/hr for 6 hr. Patients received dual antiplatlet N1unfractionised heparin (UFH), GPIIb/IIIa inhibitor. Procedure was done using iso-osmolar contrast agent. Serum creatinine value was measured at index admission, CrCl estimated using the Cockroft- Gault equation as:

CrCl (ml/min) = (140- age) × Weight (kg) ÷ 72 × S.Cr (mg/dl)

For women, multiply with 0.85.

Renal dysfunction was defined on basis of creatinine clearence.[11] KDOQI Clinical practice guidelines with creatinine clearance > 60 ml/min as normal renal function and <60 ml/min as renal dysfunction (Crcl 30-60 and Crcl < 30 was taken as two different categories).[12]

Table 1: Baseline clinical characteristics

Variables		Group A (N=60) (revascularization)	Group B (N=60) (OMT)	P value
Age mean		59.36 +_10.34	59.53 +_9.34	
Gender	**Male**	45	41	0.48
	Female	15	19	
BMI		25.26	25.15	0.14
Haemoglobin		12.35	12.38	0.47
RBS		189.4	200.5	0.14
Hypertension		35	41	0.45
Diabetes mellitus		35	36	0.76
BUN		67.8	79.3	0.36
S. creatinine		2.1	2.3	0.13
Creatinine clearance		39.9	36.1	0.06
Ejection fraction (%)		45.9	44.8	0.40
ACS- NSTEMI		40	36	0.76
STEMI		20	24	0.23
Angiography		60	44	0.23
Syntax score		27.2	31.2	0.42

BMI- body mass index; RBS – random blood sugar; BUN – blood urea nitrogen; ACS- acute coronary syndrome; NSTEMI- non ST elevation myocardial infarction;

CIN was defined as an absolute increase in the S.Cr > 0.3 mg/dl (26. mol/L) or more than 50% (1.5 times) increase in creatinine from baseline in 48-hour time frame or reduction in urine output with documented oliguria of <0.5 ml/kg/hour for 6 hours. All patients were followed up at 1 month and 12 months after index admission. Primary end point was mortality after admission till 1 year of follow up. Secondary outcomes were MACE - recurrent angina, myocardial infarction, stroke, re-hospitalization for cardiovascular cause and major bleeding till a year of follow up.

Statistical Analysis: Sample size was 60 for patients who underwent revascularization at 95% confidence interval and 6 % error. Equal number of patients were taken in medical management group to compare outcome between two group. Baseline characteristics of the patients were summarized by the two mutually exclusive groups, revascularization and OMT using absolute number and mean and standard deviation (SD). Analysis of variance was used to compare continuous variables and chi-square test or fisher's exact test was used to compare categorical variables. Any p- value < 0.05 were considered statistically significant.

RESULTS

Total of 120 patients were included in the study, out of which 104 patients underwent coronary angiography. Out of these 60 patients had coronary revascularization: 56 patients had percutaneous coronary intervention done and 4 patients underwent coronary artery bypass (CABG). Rest 44 patients were managed medically (OMT). All patients were followed up to 1 year after hospitalization. Mortality was more in OMT group than revascularization group but statistically not significant (p=0.06). Recurrent angina was more common in medical treated group 61.7% compared to intervention group 15% (p=0.00001). Recurrent angina was statistically significant in both CrCl category (CrCl 30-60, 60.5% v/s 14.9% p-0.0001 and CrCl < 30, 64.7% v/s 18.2% p-0.02 respectively). Patients who were on medical therapy were more symptomatic than revascularization group (p=.0001).

Other secondary end point including stroke, major bleeding, ST elevated myocardial infarction, heart failure was more in medically managed than revascularization group but statistically not significant. ST elevation myocardial infarction were higher in medically treated patients compared to revascularization only in moderate degree of renal dysfunction CrCl 30-60 (6 v/s 0 p-0.009) but not in CrCl < 30. Other MACE was similar in both groups in each CrCl category. Contrast induced nephropathy (CIN) was common in revascularization group compared to OMT group (p=0.003) but none of them required dialysis.

Table 2: Outcome at one year follow up

Follow up event	Revascularization group (n=60)	Optimum medical management (n= 60)	P value
All-cause mortality	1 (1.66%)	7(11.7%)	0.06
Angina	**9 (15%)**	**37 (61.66%)**	**0.00001**
Stroke	0 (0)	1 (1.6%)	1.0
Bleeding	1 (1.66%)	3 (5%)	0.61
CHF	8 (13.3%)	12 (20%)	0.31
STEMI	1 (1.66%)	6 (10%)	0.11
Asymptomatic	**40 (66.7%)**	**6(10%)**	**0.00001**
CIN	**28/60(46.6%)**	**13/44 (31.8%)**	**0.003**

CHF - Congestive Heart Failure; STEMI - ST Elevation Myocardial Infarction; CIN - Contrast Induced Nephropathy

Table 3: MACE in each CrCl category

MACE	CrCL 30-60 (n=92)			CrCL < 30 (n=28)		
	Revascularization N=49	OMT N=43	P value	Revascularization N=11	OMT N=17	P value
Death	0	3(6.9%)	0.10	1(9.1%)	4(23.2%)	0.61
Angina	**7(14.3%)**	**26(60.5%)**	**0.001**	**2(18.2%)**	**11(64.7%)**	**0.02**
Stroke	0	0	-	0	1(5.8%)	1.0
Bleeding	0	1(2.3%)	0.47	1(9.1%)	2(11.6%)	1.0
CHF	8(16.3%)	9(20.9%)	0.58	0	3(17.4%)	0.25
STEMI	**0**	**6(13.9%)**	**0.009**	1(9.1%)	0	0.39
Asymptomatic	**35(71.4%)**	**5(11.6%)**	**0.0001**	**5(45.5%)**	**1(5.8%)**	**0.01**

DISCUSSION

Cardiovascular disease is the leading cause of morbidity and mortality in patients with CKD. The optimal revascularization strategy is being debated between CABG and PCI, preferably drug eluting stent (DES) use.[13,14,15] While CABG was shown to be superior to PCI regarding long-term survival and PCI was superior for short-term survival, stroke.[13] However, recent data on new-generation DES indicate no significant difference between PCI or CABG in CKD patients. [14,15] The deleterious effect of CKD on the vasculature is reflected by occurrence of multivessel disease, small vessel disease (≤ 2.75 mm), severely calcified lesions and involvement of left main artery. We found that mortality was greater in OMT group than revascularization group but was not statistically significant. This could be attributed to the fact that majority of patients underwent PCI and only 7% had CABG in our study. Similarly previous studies have shown that ACS represent a higher-risk group that derives a greater long–term survival benefit with surgical revascularization rather than PCI. [14,16] Recently two observational studies including more than 50,000 patients, have demonstrated less benefit from coronary revascularization in patients with severe renal failure or on dialysis in term of 1-year mortality.[17,18]

Freedom from angina was better in revascularized group compared to OMT. Thus, despite the evidence of a clear benefit from coronary revascularization in high-risk ACS patients, best strategy for ACS patients with CKD remains elusive.[9,10]

CIN is by far the most common and severe procedural complication among CAD patients, independently of the beforehand presence of CKD. Baseline CKD stage, STEMI and

cardiogenic shock are the related risk factors.[19] Contrast induced nephropathy occurred in nearly half of the patients, but renal replacement therapy was not required in any of them. In our study, coronary revascularization showed a good safety profile, with no significant long-term decrease in renal function or increase in bleeding events. This is probably because of radial vascular access, less use of GPIIb/IIIa receptor blockers and dose modification of anticoagulant in our institute.

It may be more useful to intervene in recent ACS patients (<2 weeks duration) in spite of impaired renal function rather than deferring intervention on them for the fear of worsening renal function.[8,20] This study suggests that coronary angiography with the plan of revascularization is recommended after assessment of risk–benefit ratio with respect to underlying renal function. In patients undergoing PCI a new-generation DES and radial access should be the preferred approach.

LIMITATIONS

The sample size of the study was small. Our study was a single centre study, and the hospital is a tertiary care centre thus PCI or CABG availability was more to CKD patients which may not be there for patients at smaller centre. Thus, muticenteric study involving larger population are the need to the hour to develop rationale approach in these group of patients.

CONCLUSION

Patients with ACS and renal dysfunction usually have a bad prognosis. The main finding of the present study is that coronary revascularization of patients presenting with ACS and renal dysfunction is feasible, safe and associated with significantly better outcome compared with medical treatment. Dose adjustment in cardiac medications may be necessary but therapeutic nihilism may have detrimental effect and need to be overcome.

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