

## Original Research Article

# Study of risk factors associated with adverse outcome in a severe coronary artery disease (syntax score >22) with different therapeutic strategies

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## ABSTRACT

**Background:** The specific question of whether PCI or surgical treatment offers any advantage over MT in patients with stable angina and multivessel disease remains unanswered. Objective of our research was to study various risk factors which interferes the outcome of various therapeutic procedures in coronary artery disease.

**Methods:** This was prospective observational study carried out in a tertiary care center from July 2014 to July 2016. A total of 98 subjects undergoing different therapeutic strategies were followed up. Risk factors which interferes the outcome of various therapeutic procedures in coronary artery disease (CAD) were studied.

**Results:** There was a significant difference in mean SYNTAX score ( $P = 0.003$ ), urine micro albumin levels ( $P=0.006$ ), and body mass index (0.046) between those who had MACE and who did not have MACE.

**Conclusions:** The urine micro albumin >30 mg/l and highest SYNTAX score were significantly associated with MACE at 1 year in subject with severe CAD.

**Keywords:** Coronary artery disease, Microalbuminuria, SYNTAX score

## INTRODUCTION

The specific question of whether PCI or surgical treatment offers any advantage over MT in patients with stable angina and multivessel disease remains unanswered. Because PCI is unlikely to be more effective than CABG in reducing mortality or myocardial infarction (MI) in this patient population, its potential benefits are measured more readily in terms of symptomatic and functional outcomes. In this respect, several factors complicate the choices among patients who are appropriate candidates for all three therapies namely, CABG, MT or PCI. For example, the incidence of the most common adverse event- restenosis remains high despite the reduction observed after stent placement in PCI patients.<sup>1,2</sup> So, objective of our research was to

study various risk factors which interferes the outcome of various therapeutic procedures in coronary artery disease (CAD).

## METHODS

This was Observational follow up study conducted at KMC Hospital, Ambedkar Circle, Manglore, Karnataka, India within 2 years (July 2014 to July 2016).

### *Study population*

After meeting the inclusion exclusion criteria; patients admitted with acute or chronic coronary syndrome scheduled to undergo coronary angiogram was taken and underwent different treatment strategies.

### Sample size

A total of 98 subjects were followed up. It was calculated online (<http://hedwig.mgh.harvard.edu>) with minimal detectable hazard ratio as 2, duration of follow up is 1 year, power of the study 90% and level of significance 5%.

The Sample size was verified using following formula

$$N = E (\alpha, \beta, \psi) / PE$$

Where

E = Number of events  
 $\alpha$  = Level of significance  
 $\beta$  = Power of the study  
 $\psi$  = hazard ratio.

### Inclusion criteria

- Patients with angiographically documented severe CAD (SYNTAX SCORE >22) by visual assessment and documented ischemia. Ischemia will be considered for inclusion either stress testing or electrocardiographic changes or typical stable angina assessment of Canadian cardiovascular society (CCS) class II/III
- Age- 45-65 years
- Patients who has been given written informed consent.

### Exclusion criteria

- Congenital heart disease
- Valvular heart disease
- Cardiomyopathies
- Age < 45 and >65 years.

### Methodology

Approval from institutional ethics committee was taken. Patients underwent coronary angiogram for evaluation of CAD. Based on coronary interventions patients were subsequently grouped into,

- Those who underwent angioplasty
- Those who underwent coronary artery bypass graft
- Those who were medically managed.

In this study, all patients were placed on an optimal regimen consisting of a stepped care approach using nitrates, aspirin, beta blockers, CCBs, ACE inhibitors, or combinations of these drugs, unless contraindicated. Hydroxymethylglutaryl coenzyme A reductase inhibitors, along with a low-fat diet on an individual basis. Patients were then randomized to continue with aggressive

medical therapy alone or to undergo PCI or CABG concurrently with medical treatment.

Clinical details of the studied cases were noted. Adverse and other clinical events were tracked from patients which were assessed with follow up visits every 3 months until one year.

All patients were also systematically followed up by telephone interviews for 12 months which showed good reliability and validated against face to face interviews or during general clinical follow up. Patients underwent a symptom limited treadmill exercise test, according to a modified Bruce protocol, at baseline and by the end of one year, unless contraindicated.

Exercise test result were considered as positive when exertional angina developed or an ST- segment was observed with an abnormal depression (horizontal or down sloping of 1 mm for men 2 mm for women) 0.8 s after the J point. Routine examinations including ECG, 2 d echo and other relevant blood examinations. Following biochemical and clinical assays was carried out.

- Anthropometric parameters of obesity, as per WHO recommendations
- Systolic Blood Pressure
- Fasting lipid profile
- Fasting Glucose
- HbA1c
- Microalbuminuria
- Ejection Fraction
- Severity of coronary artery disease.

### Statistical analysis

A P value <0.05 will be considered statistically significant. Chi square test was used as test of significance. Statistical analysis will be performed using IBM SPSS version 20.0. Results were presented in the form of tables and Figures.

## RESULTS

A total 98 patients who had a presumptive diagnosis of CAD and who underwent coronary angiography and labelled severe CAD were added in this analysis (Table 1). These patients assigned to one of three groups CABG (n= 42, 43%), PCI (n=31; 32%), or MT (n=25; 25%). Male 54 (55%) and Female 44 (45%), almost equal in numbers (Table 1).

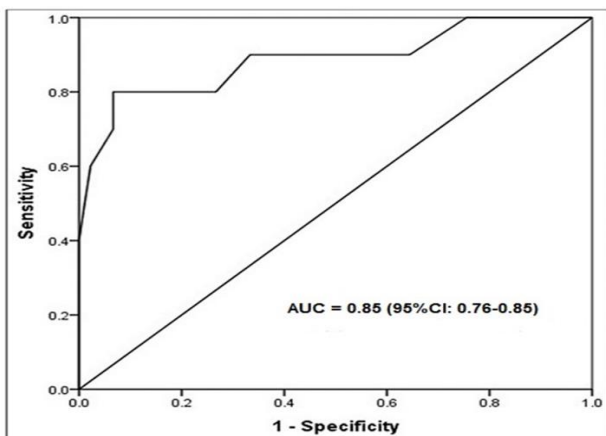
There was a significant difference in mean SYNTAX score (P = 0.003), urine microalbumin levels (P = 0.006), and body mass index (0.046) between those who had MACE and who did not have MACE (Table 2).

**Table 1: Distribution of study subjects according to gender and therapeutic procedures.**

		Advice			Total
		PTCA	CABG	Medical management	
Gender	Female	17 30.60%	18 40.90%	9 20.50%	44 100.00%
	Male	25 46.30%	13 24.10%	16 29.60%	54 100.00%
Total		42 42.90%	31 31.60%	25 25.50%	98 100.00%

**Table 2: Comparison of clinical and biochemical data according to major adverse cardia even.**

Parameter	With MACE (n=51)	Without MACE (n=47)	P value
Duration of diabetes (yrs)	8.69 ± 7.9	6.02 ± 4.51	0.074
Fasting blood glucose (mg/dl)	193.02 ± 69.36	182.96 ± 66.81	0.466
SYNTAX score	29.64 ± 5.93	26.45 ± 42.1	0.003
TC/HDL	4.42 ± 1.11	4.48 ± 1.21	0.790
LDL-C	111.97 ± 36.92	109.34 ± 36.04	0.724
Triglycerides(mg/dl)	137.47 ± 60.36	124.98 ± 62.63	0.318
HbA1c	8.04 ± 1.80	7.94 ± 1.67	0.722
Microalbumin (mg/l)	68.55 ± 16.27	28.25 ± 10.29	0.006
Body mass Index (mg/m <sup>2</sup> )	22.64 ± 2.36	23.60 ± 2.30	0.046
Waist circumference	73.56 ± 24.88	75.53 ± 28.30	0.716
Ejection fraction	44.61 ± 11.35	47.48 ± 7.88	0.214
Presence of diabetes (%)	38 (53.5%)	33 (46.5%)	0.634
Presence of hypertension (%)	28 (54.9%)	23 (45.1%)	0.555
Smoking (%)	8 (147.1%)	9 (52.9%)	0.651
Females (%)	19 (43.2 %)	25 (56.8%)	-
Males (%)	32 (59.3%)	22 (40.7%)	-



**Figure 1: Receiver operating characteristic curves showing the performance of urine Microalbumin for predicting MACE.**

The area under the curve for urine microalbumin in predicting MACE was found to be statistically significant AUC = 0.85 (95% CI: 0.76-0.85) (Figure 1). For urine microalbumin, a value of 30 mg/l had sensitivity and

specificity of 82% (95% CI: 0.73-0.89) and 78% (95% CI: 0.63-0.76) respectively (Figure 1).

Table 3 shows the univariate cox-proportional hazard model for prediction of MACE at one year in subjects with severe and complex CAD.

Here only SYNTAX score 0.054, Microalbuminuria >30 mg/l having p value <0.001, Mode of treatment and Body mass index >23 Kg/m<sup>2</sup> are p value, 0.002 and 0.019 respectively found strong relationship with MACE.

So, those variables with p value <0.20 were included for multivariate cox proportional hazard model. After the adjustment for potential confounder's in multivariate cox proportional hazard model, the urine microalbumin >30 mg/l (adjusted hazard ratio (hr): 35.81, 95% ci: 2.14-12.53, P <0.001) and baseline severity of cad (syntax score) (adjusted hazard ratio (hr): 3.78, 95% ci: 1.65-9.75, p=0.005) were significantly associated with mace at one year in subjects with severe and complex cad (Table 4). The other conventional risk factors of cad were not significant (Table 4).

**Table 3: Univariate Cox regression analysis for the relationship between adverse cardiovascular events and other conventional risk factors in subjects with severe and complex CAD.**

Variables	B	Hazard ratio	p value
SYNTAX Score	0.048	1.049	0.054
Microalbumin >30 mg/l	1.86	5.76	<0.001
Diabetes	0.661	1.93	0.072
Mode of Treatment (PTCA/CABG/Medical)	0.803	2.23	0.002
TC/HDL >5	0.089	1.09	0.795
LDL >100 mg/dl	0.322	1.38	0.172
Body mass index >23 kg/m <sup>2</sup>	-0.658	0.518	0.019
Waist circumference (cm)	-0.275	0.622	0.297
Hypertension	-0.195	0.823	0.487
Smoking	0.041	1.04	0.909
Gender (Male/Female)	0.361	1.43	0.214
Age (years)	-0.057	0.945	0.061

Tc/hdl- total cholesterol/ high density lipoprotein ratio; ldl – low density lipoprotein.

**Table 4: Multivariate Cox regression analysis showing the independent predictors of adverse cardiovascular events in subjects with severe and complex CAD: result of a one-year follow-up.**

Variables	B	Hazard ratio	p value
Microalbumin >30 mg/l	2.34	5.81	<0.001
SYNTAX Score	1.39	3.78	0.005
Diabetes	0.51	1.67	0.248
Mode of treatment (PTCA)	0.85	1.92	0.122
Mode of Treatment (Medical)	1.06	2.01	0.086
LDL >100 mg/dl	0.24	1.27	0.486
Body mass index >23 kg/m <sup>2</sup>	-0.22	0.80	0.533

LDL-Low Density Lipoprotein.

## DISCUSSION

The great singer Whitney Houston posed a question over 25 years ago that many still ponder today. “Where,” she asked, “do broken hearts go?” Of course, her classic song asks us to imagine a destination for the pain wrought by the dissolution of love. Physicians, however, have more concrete possibilities in mind when asking where to take the hurting center of our emotional and physiologic lives: the cardiac catheterization lab versus the operating room. That is, for patients with multi-vessel coronary artery disease (CAD) who require revascularization, should first-line treatment be PCI or CABG? Our study done at a single institution, to study various risk factors which

interferes the outcome of various therapeutic procedures in coronary artery disease (CAD).

In this study, MACE at 1 year with different therapeutic strategies, with clinical variables like, DM, IHD (previous history), smoking and gender having no significant association but HTN in study group has minimal association with MACE.

The present study has demonstrated no significant clinically relevant differences among the 3 therapeutic strategies in relation to cardiac related death. However, refractory angina requiring further revascularization is higher in the PCI compared with the CABG group. Furthermore, the MT patients had less relief from symptomatic angina than patients who underwent CABG or PCI. Although a placebo effect related to the invasive nature of former modalities could not be ruled out, we should emphasize that these difference in angina status were paralleled by a highly significant reduction in the rate of objective ischemia in both CABG and PCI compared with MT. This trial also found a strong association between CABG and the protective effect against primary end points. CABG reached a significant reduction in non-fatal MI, death, or additional revascularization compared with MT, regardless of sex, smoking, cholesterol, need for medications, previous MI, ventricular function, hypertension, diabetes mellitus, angina status, and number of diseased vessels.

This study and MASS II at five-year, CABG is superior to MT for relief of angina and less objective ischemia. Moreover, CABG reached an independent significant reduction in of major adverse cardiac events compared with MT. These results provide evidence that improved perioperative management and intraoperative techniques over time result in a reduction in mortality compared with previous results of CABG trials, as well as these better outcomes compared with MT and PCI found in our study.

This study sought to identify factors affecting MACE in patients who underwent PCI or CABG or MT in severe CAD. Although half of patients were men, sex had no significant effect on MACE. However, some studies have found higher mortality rates in women than in men.

Diabetes mellitus was identified as an independent risk factor for adverse clinical events and restenosis and lower rates of event-free survival than nondiabetic patients. Diabetes mellitus confers a higher incidence of death, recurrent myocardial infarction, restenosis, and repeat revascularization rates. Surprisingly, authors found diabetes or high fasting blood sugar level, HbA1c is not correlated with increased risk of MACE in patients who received revascularization or MT.<sup>3</sup> In other words, diabetes is not at all significantly more prevalent in the group with complications than in the control group. Patients with diabetes mellitus have increased morbidity and mortality after coronary revascularization. A study by Elezi et al, analyzed a consecutive series of 715 patients

with diabetes and 2,839 patients without diabetes after successful stent placement. At 1-year follow-up, event-free survival was significantly lower in diabetic than in non-diabetic patients (73.1% versus 78.5%).<sup>3</sup>

In this study, smoking did not have any effects on MACE. Smoking is a major risk factor for coronary artery disease (CAD) and risk of future major adverse cardiac events (MACEs).<sup>4-9</sup> While the increased in risk of events applies to current smokers, several previous studies have shown that individuals who have quit smoking have risk of future MACE that is similar to individuals who have never smoked.

High arterial blood pressure is a risk factor for coronary artery disease. However, authors do not find significant differences in level of blood pressure between MACE and non-MACE groups.

Despite the fact that hyperlipidemia is a risk factor for coronary artery disease, it had no significant effects on the incidence of MACE in this study.

The SYNTAX score is an angiographic tool to help cardiologists, interventionists and surgeons to grade the complexity of coronary artery lesions. A higher SYNTAX score indicates a more complex condition as well as worse prognosis in patients undergoing contemporary revascularization especially with PCI.<sup>10</sup> However, its value for predicting early and late mortality and complications is still a question mark. Although some authors have reported an acceptable predictive power for the SYNTAX score concerning major adverse cardiac and cerebrovascular events following revascularization, there are still few precious data on its predictive value for early or late mortality.<sup>11</sup>

Present study findings suggest that the SYNTAX scoring model can play a major role in predicting short-term outcomes following PCI or CABG or MT in patients with severe CAD.

Body mass index, waist circumferences are independent predictor of CAD but no correlation with these factors with respect to MACE in our analysis.

Low ejection fraction is strong predictor for adverse outcome in CAD with or without revascularization, but our data had no correlation of LV EF with MACE.

In our study, an association between microalbuminuria and MACE was demonstrated, which confirms earlier evidence on the impact of microalbuminuria on cardiovascular risk. Furthermore, in line with an earlier angiographic study.<sup>12</sup> Microalbuminuria was most frequently present in subjects who had severe CAD at CAG during follow-up. Whether microalbuminuria can be regarded as an appropriate screening tool in asymptomatic populations is subject to future

investigation. This observation is matching with Prevend cohort.

## CONCLUSION

A higher SYNTAX score indicates a more complex condition as well as worse prognosis in patients undergoing contemporary revascularization especially with PCI. The urine micro albumin >30 mg/l were significantly associated with MACE at 1 year in subject with severe CAD.

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*Ethical approval: The study was approved by the Institutional Ethics Committee*

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