Journal of Integrative Cardiology

Research Article

ISSN: 2058-3702

Outcomes of different patterns of percutaneous revascularization for non-ST-segment elevation acute coronary syndrome patients with multivessel coronary artery disease

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Abstract

Background: The incidence of multivessel disease (MVD) among patients presenting with non-ST-segment elevation acute coronary syndrome (NSTE-ACS) is very high, and the optimum revascularization strategy is debatable. The aim of this study was to evaluate the different patterns of percutaneous revascularisation (PCI) for NSTE-ACS patients with MVD and to determine the long-term outcomes in terms of major adverse cardiac and cerebrovascular events (MACCE).

Methods: This study included 490 patients who presented at our hospital for NSTE-ACS with MVD, from January 2008 to June 2016. Based on revascularization patterns, the patients were divided into 3 groups: Group I: 211 patients underwent incomplete revascularisation (IR) for the culprit vessel only, Group II: 249 patients underwent complete revascularization (CR) for both, culprit and non-culprit vessels in the same setting and Group III: 30 patients underwent complete revascularisation for both culprit and non-culprit vessels in different settings. The primary study endpoint was the incidence of MACCE, which was defined as a composite of cardiac death, all cause death, re-infarction, re-hospitalisation for unstable angina, need for repeat coronary revascularization, and stroke in-hospital and at a minimum period of 6 months.

Results: There was no statistically significant difference between the 3 groups in terms of the in-hospital outcomes. The composite MACCE endpoint at 6 months (death, re-infarction, need for revascularization and stroke) was higher in group I than in the other 2 groups. The overall MACCE were 50% higher in group 1 compared to the other 2 groups (P<0.001). The composite MACCE endpoint at 6 months was higher in group III than in group II (16% *vs.* 12.8% respectively), but without statistical significance. Cardiac death occurred in 11 patients (6.3%) in group I, and in 4 patients (1.9%) in group II; however, there was no cardiac death in group III (P=0.045). Stroke occurred only in 1 patient (0.6%) in group I. There was no statistically significant difference in the incidence of stroke between the 3 groups (P=0.485). Re-infarction occurred in 19 patients (10.8%) in group I, 12 patients (5.7%) in group II, and 4 patients (16%) in group III (P=0.081). The need for revascularization procedures was very high in group I (76 patients; 43.2%) compared to both group II (17 patients; 8.1%), and group III (4 patients; 16%) (P<0.001). In group I we also calculated the RSS (RSS) and there was a higher incidence of MACE with RSS >8 compared to RSS ≤ 8 (61% *vs.* 41.4% respectively) (P=0.010)

Conclusion: In patients of NSTE-ACS with MVD, complete revascularisation either in the same setting or in a staged manner is better compared to only culprit vessel PCI in terms of long term total MACCE, cardiac death and the need for revascularisation. There was no difference in MACCE outcomes between revascularisation in the same setting and staged revascularisation. In case of incomplete revascularisation, RSS is a good and reliable predictor of total MACCE.

Introduction

Cardiovascular diseases are currently the leading cause of death in industrialised countries, and a similar situation is expected to occur in the developing countries by 2020. Among these, coronary artery disease (CAD) is the most prevalent manifestation and is associated with high mortality and morbidity [1]. Registry data consistently show that NSTE-ACS is more frequent than ST segment elevation (STE)-ACS [2]. The annual incidence is 3 per 1000 inhabitants but varies between countries [3]. Long term follow-up has shown that death rates are higher among patients with NSTE-ACS than in those with STE-ACS, with a two-fold difference at 4 years [4]. This difference in the death rates at mid and long-term follow up might be due to different patient profiles since NSTE-ACS patients tend to be older, with higher number of co-morbidities, especially diabetes and renal failure. Outcomes from epidemiological observations suggest that treatment strategies for NSTE-ACS need to focus not only on the acute phase, but also provide equal emphasis on longer term management [5].

The recent guidelines for the management of patients presenting with NSTE-ACS, indicate that there are no prospective randomised trials comparing complete versus staged revascularization (i.e. complete *vs.* incomplete) and the timing (i.e. simultaneous *vs.* staged) of revascularization in such patients [6,7]. A complete revascularisation strategy for significant lesions in patients of NSTE-ACS with multivessel disease (MVD) is based on two considerations. One, several studies showing the benefit of early intervention compared to the conservative approach in patients with NSTE-ACS, mandated a complete revascularization strategy, irrespective of the identification

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Key words: *multivessel disease, revascularization, coronary artery disease*

Received: January 28, 2019; **Accepted:** February 05, 2019; **Published:** February 08, 2019

and/or treatment of the culprit lesion [8-10]. Secondly, multiple PCI and NSTE-ACS trials have shown poor prognostic outcomes of incomplete revascularization. Accordingly, an RSS >8 has been shown to be independently associated with a poor 30-day and 1-year prognosis, including higher mortality after PCI in patients with moderate and high-risk. [11,12].

Aim of the study

The aim of the study was to compare the different patterns of PCI in NSTE-ACS patients with MVD, and to determine the outcomes in terms of the major adverse cardiac and cerebrovascular events (MACCE) like cardiac death, re-infarction, stroke, the need for revascularisation, and major bleeding.

Methods

This study included 490 patients of NSTE-ACS with MVD who presented at our hospital from January 2008 until June 2016. Based on the revascularization strategies, the patients were divided into 3 groups: Group I: 211 patients underwent incomplete revascularization (IR) for the culprit vessel only; Group II: 249 patients underwent complete revascularization (CR) for both culprit and non-culprit vessels in the same setting; and Group III: 30 patients underwent complete revascularization for both culprit and non-culprit vessels in different settings. Coronary angiography and the PCI procedure including pre-procedural preparation, PCI procedure details, materials used, intra-procedure complications, and post-PCI management were documented. Baseline SYNTAX score and RSS were also calculated. The primary endpoint of the study was the incidence of MACCE, which was defined as a composite of cardiac death, any cause death, re-infarction, re-hospitalisation for unstable angina, the need for repeat coronary revascularization, and stroke while in hospital and at a minimum of 6 months follow up.

Results

Patient Characteristics: All groups were well matched with respect to the demographic and clinical characteristics; the baseline characteristics of all groups are presented in Table 1.

Procedural characteristics of the studied population: There was no statistically significant difference between the 3 groups in terms of the percentages of LM, LAD and RAMUS as the target vessel. Group I and group III had a greater number of patients with significantly diseased LCX and RCA, than group II and this difference was statistically significant (P=0.027 for LCX) and (P<0.001 for RCA). GP IIb/IIIa inhibitors were administered to 72 (34.1%) patients in group I, 74 (29.7%) in group II, and 13 (43.3%) patients in group III and there was no statistically significant difference in the percentages between the 3 groups (P=0.52). Chronic total occlusion (CTO) lesions were found in 107 (50.7%) patients in group I, 55 (22.1%) patients in group II, and 10 (33.3%) patients in group III. The difference in percentage of CTO lesions between group I and group II was statistically significant (P<0.001). Long lesions were found in 67 (31.7%) patients in group I, 73 (29.3%) patients in group II, and 13 (43.3%) patients in group III; however, there was no statistically significant difference between the 3 groups (P=0.153). The mean syntax score was higher in group I (16.9; range 4-50) than in group II (13.8; range 4-39) and the difference was statistically significant (P<0.001). In group III, the mean syntax score

Table 1. Baseline Characteristics of the Studied Populations

	Group I Culprit only PCI (n=211)	Group II Total Revascularisation (n=249)	Group III Staged Revascularisation (n=30)	P Value
Age, yrs Mean ± SD.	64.6 ± 10.42[a]	63.02 ± 9.9[a,b]	58.73 ± 8.96 [b]	0.008*
Sex				
Male	160(75.8%)	195(78.3%)	28(93.3%)	0.094
Female	51(24.2%)	54(21.7%)	2(6.7%)	
Medical history				
DM	118(55.9%)	133(53.4%)	17(56.7%)	0.843
HTN	139(65.9%)	149(59.8%)	19(63.3%)	0.410
Hypercholesterolaemia	72(34.1%)	80(32.1%)	10(33.3%)	0.902
Current smoker	28(13.3%)	36(14.5%)	7(23.3%)	0.342
Previous MI	16(7.6%)	11(4.4%)	2(6.7%)	0.352
Previous PCI	44(20.9%)	42(16.9%)	5(16.7%)	0.528
Risk stratification				
GRACE score				
Mean ± SD.	127.5 ± 31[a]	121.6 ± 30[a,b]	113.3 ± 24[b]	0.02*
CRUSADE score				
Mean ± SD.	26.7 ± 13[a]	25.5 ± 13[a,b]	20.9 ± 11 [b]	0.04*
Lab investigation				
Positive Troponin	127(60.2%)	155(62.2%)	21(70%)	
Creatinine				0.575
Normal RFT	177(83.9%)	212(85.1%)	25(83.3%)	
CKD	33(15.6%)	34(13.7%)	5(16.7%)	MCP=0.834
CKD on HD	1(0.47%)	3(1.2%)	0(0%)	
LV EF%	58.8 ± 11.36[a]	61.72 ± 8.87[b]	60.8 ± 11.15[a,b]	0.016*
MR	211	249	30	
No	164(77.7%)[a]	218(87.6%)[b]	21(70.0%)[a]	0.004*
Mild	25(11.8%)[a]	23(9.2%)[a]	9(30.0%)[b]	0.004*
Moderate	12(5.7%)[a]	5(2.0%)[b]	0(0.0%)[b]	0.056
Severe	10(4.7%)[a]	3(1.2%)[b]	0(0.0%)[b]	0.041*

*statistically significant at p <.05, Using F test. a,b: similar letters mean no significant difference between groups , different letters means significant difference between groups using post hoc test. MCP: Monte carlo significance test.

was 15 (range 4-30) without statistical significance with the other 2 groups. The number of stents inserted was lowest in group I with a mean of 2 (range 1-5), followed by group II with a mean of 2 (range 1-6), and highest in group III with a mean of 3.5 (range 2-7). There was a significant statistical difference between the 3 groups with respect to the number of stents used per patient (P<0.001). In group I patients, 87 bare metal stents (BMS) (23.6%) and 282 drug eluting stents (DES) (76.4%) were used; in group II patients, 112 BMS (18.2%) and 502 DES (81.8%) were used; while in group III patients 8 BMS (7%) and 107 (93%) were used. There was no statistically significant difference between the 3 groups with respect to the use of BMS (P=0.923). More number of DES were used in group II than in group I (P=0.006).

Syntax score post-procedure (RSS): The mean RSS in group I was 7 (range 1-30), which was significantly higher than that of the other 2 groups. In group II the mean RSS was 0 (range 0-17), and in group III the mean RSS was 1.5 (range 0-15). The difference in RSS between group I and group II was statistically significant (P<0.001). All data of the procedural characteristics of the studied population are summarised in Table 2.

In-hospital outcomes: In group I, 0.5% of the patients required revascularization (TVR), 0.5% developed heart failure, 0.5% developed cardiogenic shock (due to post-PCI pericardial effusion, and pericardiocentesis was performed), and 1.9% developed arrhythmia (AF in 2 patients, ventricular tachycardia in 1 patient and ventricular bigeminy in 1 patient). Additionally, 0.5% of the patients developed major bleeding, 0.9% patients developed minor bleeding, and 2.8% patients developed contrast induced nephropathy CIN. In group II, 0.4% of the patients developed a re-infarct, 0.4% patients required revascularization (TVR), 0.8% patients developed heart failure (2 patients, of which 1 required mechanical ventilation), 1.6% patients developed cardiogenic shock, 1.2% patients developed major bleeding, 0.4% patients developed minor bleeding and 3.2% patients developed CIN (8 patients, 2 of them needed HDF). There was no in-hospital complication in group III. However, there was no statistically significant difference between the 3 groups with respect to the in-hospital complications. The data of in-hospital outcomes are summarised in Table 3.

Follow-up (at least 6 months follow-up): The composite MACCE (Major Adverse Cardiac and Cerebrovascular Events) endpoint at 6 months (death, re-infarction, need for revascularization and stroke) was higher in group I than in the other 2 groups, the overall MACCE were 50% higher in group 1 compared to the other 2 groups (P<0.001). The composite MACCE endpoint at 6 months was higher in group III than in group II 16% *vs.* 12.8% respectively, but no statistical significance was found.

Cardiac death occurred in 11 patients (6.3%) in group I, and in 4 patients (1.9%) in group II, but none in group III. The difference in cardiac death between group I and group II was statistically significant (P=0.045). Stroke occurred only in 1 patient (0.6%) in group I. No statistical significance was seen between the 3 groups with respect to

Table 2. Procedural Characteristics According to randomised allocation. *statistically significant at p<0.05 using Kruskal Wallis test (H). **statistically significant at p<0.05 using Pearson Chi square test. a,b,c :similar letters mean no significant difference between groups , different letters means significant difference between groups using post hoc test

	Group I Culprit only PCI (n=211)	Group II Total Revascularisation (n=249)	Group III Staged Revascularisation (n=30)	P Value
Target vessels				
Left Main	13(6.2%)	7(2.8%)	1(3.3%)	0.202
LAD	185(87.7%)	205(82.3%)	24(80%)	0.193
RAMUS	22(10.4%)	28(11.2%)	2(6.7%) 25(83.3%)[a]	0.778
LCX	147(69.7%)[a]	155(62.2%)[b]	24(80%)[a]	0.027*
RCA	166(78.7%)[a]	108(43.4%)[b]		<0.001*
Total no of Stent/patient	2(1-5) [a]	2(1-6)[b]	3.5(2-7) [c]	<0.001*
Stent type				
BMS	87(23.6%)	112(18.2%)	8(7%)	0.923
DES	282(76.4%)[a]	502(81.8%)[b]	107(93%)[a,b]	0.006**
Presence of CTO	107(50.7%)[a]	55(22.1%)[b]	10(33.3%)[a,b]	<0.001**
Presence of long lesions	67(31.7%)	73(29.3%)	13(43.3%)	0.153
Use of GP IIb/IIIa	72(34.1%)	74(29.7%)	13(43.3%)	0.52
Syntax score (pre-procedural)	16.9(4-50)[a]	13.8(4-39)[b]	15(4-30)[a,b]	<0.001*
Syntax score (post-procedural)	7(1-30)[a]	0(0-17)[b]	1.5(0-15)[a,b]	<0.001*

Table 3. In hospital outcomes

	Group I Culprit only PCI (n=211)	Group II Total Revascularisation (n=249)	Group III Staged Revascularisation (n=30)	P Value
Cardiac death	0(0%)	0(0%)	0(0%)	-
Re-infarction	0(0%)	1(0.4%)	0(0%)	MCP=1
Need for revascularisation (TVR)	1(0.5%)	1(0.4%)	0(0%)	MCP=1
Heart failure	1(0.5%)	2(0.8%)	0(0%)	MCP=1
Cardiogenic shock	1(0.5%)	4(1.6%)	0(0%)	MCP=0.79
Arrhythmia	4(1.9%)	0(0%)	0(0%)	MCP=0.07
Major bleeding	1(0.5%)	3(1.2%)	0(0%)	MCP=0.71
Minor bleeding	2(0.9%)	1(0.4%)	0(0%)	MCP=0.67
CIN	6(2.8%)	8(3.2%)	0(0%)	MCP=0.61

MCP: Monte carlo significance test

stroke (P=0.485). Re-infarction occurred in 19 patients (10.8%) in group I, 12 (5.7%) in group II, and 4 patients (16%) in group III. No statistical significance was seen between the 3 groups with respect to re-infarction (P=0.081). Revascularization was required in 76 patients (43.2%) in group I, 17 patients (8.1%) in group II, and 4 patients (16%) in group III. The differences were statistically significant (P<0.001). The need for either TVR OR non-TVR was much higher in group I than in the 2 other groups and the difference was statistically significant (P<0.001). Group I required earlier revascularization compared to the 2 other groups. The mean time for revascularization was 35.8 ± 20.1 months in group I, 41.2 ± 21.2 months in group II, and 42.1 ± 24.4 months in group III (P=0.03).

Heart failure occurred in 10 patients (5.7%) in group I, 6 patients (2.9%) in group II and 0 in group III. There was no statistically significant difference between the 3 groups (P=0.216). Arrhythmia occurred in 3 patients (1.7%) in group I, 4 patients (1.9%) in group II, but in none in group III. No statistically significant difference was seen between the 3 groups (MCP=1). Major bleeding occurred in 2 patients (1.1%) in group I, 2 patients (1%) in group II, but in none in group III. No statistically significant difference was seen between the 3 groups (MCP=1). Minor bleeding occurred in 2 patients (1%) in group II, and in none in the other 2 groups. No statistically significant difference was seen between the 3 groups in terms of minor bleeding (MCP=0.57). All the follow up data are summarized in Table 4 and Figures 1 and 2.

Relationship between the RSS and MACCE, cardiac death, re-infarction, stroke, need for revascularization in the only culprit vessel PCI group: We classified the only culprit vessel PCI group according to the RSS into 2 subgroups, the first subgroup comprising 99 patients with an RSS ≤8 and the second subgroup comprising 77 patients with an RSS>8. We compared the groups for incidence of total MAACE, cardiac death, re-infarction, stroke and the need for revascularization either TVR or Non-TVR after 6 months. We found a statistically significant relationship between the RSS and total MAACE after 6 months. The incidence of total MACCE was higher in the second subgroup than in the first subgroup with a statistical significance (61% and 41.4% respectively, P=0.010).

We found a statistically significant relationship between RSS and the rate of re-infarction after 6 months; the incidence of re-infarction was higher in the second subgroup compared to the first (19.5% and 4% respectively, P=0.001). We found a statistically significant relationship between the RSS and the need for revascularization after 6 months. The need for revascularization was higher in the second subgroup than in the first (54.5% and 34.3% respectively, P=0.007). We found

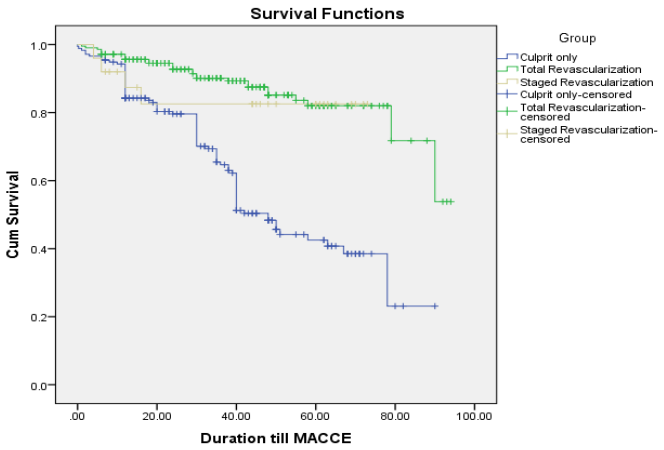

Figure 1. Kaplan-Meier survival curve for MACCE

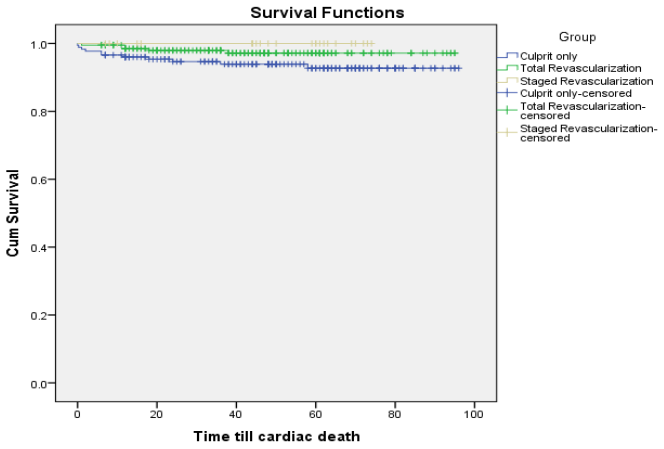

Figure 2. Kaplan-Meier survival curve for Cardiac death

Table 4. 6 months at least Clinical Events according to randomised allocation

	Group I Culprit only PCI (n=176) Missed=35	**Group II Total Revascularisation (n=211)** Missed=38	**Group III Staged Revascularisation (n=25)** Missed=5	**P Value**
Total MACCE	88(50.0%)[a]	27(12.8%)[b]	4(16%)[b]	<0.001*
Cardiac death	11(6.3%)[a]	4 (1.9%)[b]	0(0%)[a,b]	0.045*
Reinfarction	19(10.8%)	12(5.7%)	4(16%)	0.081
Stroke	1(0.6%)	0(0%)	0(0%)	0.485
Need for Revascularisation	76(43.2%)[a]	17(8.1%)[b]	4(16%)[b]	<0.001*
TVR	27(15.3%)[a]	8(3.8%)[b]	3(12%)[a,b]	<0.001*
TLR	18(10.2%)[a]	6(2.8%)[b]	2(8%)[a,b]	0.011*
NON-TLR	9(5.1%)	3(1.4%)	1(4%)	0.125
NON TVR	42(23.9%)[a]	12(5.7%)[b]	2(8%)[a,b]	<0.001*
Time till revascularisation	35.8±20.1[a]	41.2±21.2[b]	42.1±24.4[a,b]	0.03*
Heart Failure	10(5.7%)	6(2.9%)	0(0%)	0.216
Arrhythmia	3(1.7%)	4(1.9%)	0(0%)	MCP=1
Major bleeding	2(1.1%)	2(1%)	0(0%)	MCP=1
Minor bleeding	0(0%)	2(1%)	0(0%)	MCP=0.57

*statistically significant at p <.05 using F test. **statistically significant at p <.05 using Pearson Chi square test. -a,b: similar letters mean no significant difference between groups , different letters mean significant difference between groups using post hoc test. -MCP: Monte Carlo significance test

a statistically significant relationship between the RSS and Non-TVR after 6 months; the incidence of Non-TVR was higher in the second subgroup than in the first with statistical significance (31.2% and 18.2% respectively, P=0.045).

Thus, there was a statistically significant trend towards a higher rate of MACCE, re-infarction, the need for revascularization and non-TVR in the only culprit vessel PCI subgroup of patients with RSS>8. Considering only the (death/re-infarction), the outcomes were in favor of patients with RSS ≤8 with statistical significance (24.7% and 10.1% respectively, P=0.010). All data are summarised in Table 5.

Discussion

In recent times, PCI has become one of the most frequently performed therapeutic interventions in medicine, and the progress in technology has resulted in a steady decline of periprocedural adverse events, coupled with excellent outcomes [13]. A consensus on the best possible revascularization approach, taking into consideration the social and cultural context, and frequent interactions between cardiologists and cardiac surgeons, referring physicians, or other specialists as appropriate, is necessary [14]. Ultimately, risk stratification can be used as a guide, while clinical judgement and multidisciplinary dialogue (The Heart Team) continue to remain essential [15]. The distribution of PCI *vs.* CABG in patients with multivessel disease suitable for revascularization is approximately 80% *vs.* 20% [16]. The revascularization strategy in patients with multivessel CAD should be determined early by the Heart Team, based on the patient's clinical status as well as the severity and distribution of the CAD and the characteristics of the lesion [17].

The SYNTAX score has proven to be strongly predictive of death, myocardial infarction and TVR [17]. The 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation have mentioned [18], that there is a lack of prospective randomized trials about complete versus staged revascularization, addressing the type (i.e. complete *vs.* incomplete) and timing (i.e. simultaneous *vs.* staged) of revascularization in NSTE-ACS.

A complete revascularization strategy for significant lesions should be pursued in multivessel disease patients with NSTE-ACS based on two considerations. First, several studies proving the benefit of early intervention compared to the conservative approach in patients with NSTE-ACS mandated a complete revascularization strategy, irrespective of the identification and/or treatment of the culprit lesion [8-10]. Second, multiple PCI and NSTE-ACS trials have shown a poor prognosis following incomplete revascularization. Accordingly, an RSS >8 has been shown to be independently associated with a poor 30-day and 1-year prognosis, including higher mortality after PCI in patients with moderate and high-risk ACS. The decision to treat all significant lesions in the same setting or in a staged manner should be based on clinical presentation, comorbidities, complexity of the coronary anatomy, ventricular function, revascularization modality, and patient preference [11,12].

In our study the mean age of the patients was 61.6 years, which was not very different from that in other studies published in the literature in the developed countries. An exception was the SMILE trial [19], where the mean age was 72.5 years. This indicates an earlier occurrence of coronary artery disease in our country due to the higher prevalence of some CAD risk factors like diabetes and hypertension in our country, reaffirming the urgent need for strict control of these risk factors.

In our study the mean age in group I was higher than that in group II and III with statistical significance; the same was found in the study by M.G. Bourassa, *et al.* [20], where patients with incomplete revascularization were older. This difference might be explained by a higher prevalence of risk factors, co-morbidities, and a higher risk of bleeding in group I patients. Hence, in this subgroup of older patients only the culprit vessel stenting might be a better strategy.

We also found a higher prevalence of diabetes in our study (56.7%) compared to other studies like the SMILE trial Gennaro Saradella, *et al.* [19] (39.5%) and those by Corrado Tamburino, *et al.* [21] (35%), Giuseppe Mariani, *et al.* [22] (26%), Shubrooks Jr, *et al.* [23] (22%). This indicates the significant impact of diabetes mellitus as a CAD risk factor in our study. The prevalence of hypertension in our study was similar to that in the other studies, ranging from 42% to 73% and reaffirming the impact of hypertension as CAD risk factor worldwide. The mean GRACE risk score in our study was (120.8), which was lower than that in the SMILE trial [19] (175.5). This can be explained by a higher mean age in the SMILE trial; [19] in our study as well, the GRACE risk score and CRUSADE risk score for bleeding were higher in group I where the mean age was higher than that of group III.

In the present study, the mean syntax score was found to be higher in group I (16.9; range 4-50) than in group II (13.8; range 4-39); this was due to more complex coronary lesions in group I. Higher the complexity of lesions, better the strategy of targeting only the culprit lesion. In the SMILE Trial Gennaro Saradella, *et al.* [19] in one-stage PCI group, the mean syntax score was 16 (ranging from 14 to 18), while in the multi-stage PCI group, the mean syntax score was 15 (ranging from 14 to 18) without any statistical significance.

Table 5. Relation between RSS with different parameters in group I

	RSS		χ^2	P
	≤8 (n=99)	>8 (n=77)		
Total MACCE	41(41.4%)	47(61.0%)	6.672*	0.010*
Cardiac death	6(6.1%)	5(6.5%)	0.014	FEp=1.00
re-infarction	4(4.0%)	15(19.5%)	10.722*	0.001*
Cardiac death + re-infarction	10(10.1%)	19(24.7%)#	6.685*	0.010*
Stroke	0(0.0%)	1(1.3%)	1.293	FEp=0.438
Need for revascularisation	34(34.3%)	42(54.5%)	7.205*	0.007*
TVR	17(17.2%)	10(13.0%)	0.584	0.445
TLR	10(10.1%)	8(10.4%)	0.004	0.950
Non TLR	7(7.1%)	2(2.6%)	1.786	0.302
Non TVR	18(18.2%)	24(31.2%)	4.021*	0.045*

χ^2, p: χ^2 and p values for Chi square test to compare the two groups. FE: Fisher Exact for Chi square test to compare the two groups *: Statistically significant at P ≤ 0.05. #: Patient number 308 had a Cardiac death and re-infarction in the RSS>8 subgroup

In our study there was no statistically significant difference in the in-hospital outcomes between the groups, which might be due to the lower GRACE risk score in our patients compared to that in other studies. This finding was similar to that in studies by Corrado Tamburino, *et al.* [21]. Edward L. Hannan, *et al.* [24] and Giuseppe Mariani, *et al.* [22] However, our findings were in contrast with those of M. G. Bourassa, *et al.* [20] who reported a higher incidence of emergency and elective CABG in the incomplete revascularization group and Hawranek M, *et al.* [25] who reported a lower in-hospital mortality in the complete revascularization group. Our study findings were also in contrast to that of Ljsselmuiden, *et al.* [26] who reported that the success rate was higher in the culprit vessel PCI group than in the complete revascularization group. Shubrooks, *et al.* [23] reported a lower frequency of vascular complications (thrombosis or pseudoaneurysm requiring surgery or bleeding requiring transfusion) with ad hoc procedures, although in our study no statistically significant difference between the groups was seen with respect to major or minor bleeding.

A higher incidence of total MACCE and the need for revascularization (TVR or Non-TVR) at 6 months follow-up were seen in the only culprit vessel stenting group than in the total or the staged revascularization groups, with statistical significance. This was in line with that reported in studies like the SMILE Trial Gennaro Saradella, *et al.* [19] and those by Corrado Tamburino, *et al.* [21], Van den Brand, *et al.* [27], M.G. Bourassa, *et al.* [20], Ljsselmuiden, *et al.* [27] and Nikolsky E, *et al.* [28] where total MACCE and/or the need for revascularization was more in the incomplete revascularization group with a statistical significance. However, our finding was in contrast with that of Yang HH, *et al.* [29] and Guiseppe Mariani, *et al.* [22] where the total MACCE and/or the need for revascularization were similar in the incomplete and complete revascularization groups. In our study there was a higher incidence of cardiac death in the culprit only stenting group than in the total or the staged revascularization groups, with a statistical significance, at 6 months follow-up.

This finding was in line with studies by Corrado Tamburino, *et al.* [21], Edward L.Hannan, *et al.* [24], and M.B.Iqbal, *et al.* [30], where a higher incidence of cardiac death was seen in the incomplete revascularization group with a statistical significance, but was in contrast with other studies as those by HH YANG, *et al.* [29], Guiseppe Mariani, *et al.* [22] and Hawranek M, *et al.* [25] where the incidence of cardiac death was similar in the incomplete and complete revascularization groups. In our study there was no statistically significant difference in the incidence of myocardial infarction between the groups at 6 months follow up; this could indicate good compliance to medical treatment in our patients.

This finding was in line with some studies like the SMILE Trial Gennaro Saradella, *et al.* [19] and those by Yang HH, *et al.* [29] and Guiseppe Mariani, *et al.* [22] but was in contrast with studies by Corrado Tamburino, *et al.* [21], and Palmer N. D, *et al.* [31] where a higher incidence of myocardial infarction was found in the incomplete revascularization group, with statistical significance. It was noted in two studies by Edward L. Hannan, *et al.* [24] and Goldstein CL, *et al.* [32] that complete revascularization had poorer clinical outcomes including mortality, in patients with congestive heart failure and CCS class IV; hence, complete revascularization was not recommended in this category of patients.

In our study, there was a higher rate of MACCE, re-infarction, need for revascularization and non-TVR in the only culprit vessel PCI subgroup of patients with an RSS>8. When considering only the (death/re-infarction), the outcomes were better in patients with an RSS ≤8 (24.7% in the second subgroup and 10.1% in the first subgroup, P=0.010).

Witberg, *et al.* [33] studied the incremental impact of RSS on long-term clinical outcomes in 148 consecutive patients with MVD treated by PCI with triple vessel/left main CVD. Clinical outcomes at 3 years were collected, and the SS and rSS were calculated. The rSS at a cutoff value determined according to ROC curve fitted for 3 years MACCE to determine which definition has the strongest correlation with long-term outcomes. Witberg, *et al.* [33] found that rSS ≤ 8 was associated with significant reductions in the 3-year MACCE (19.4 *vs.* 51.1%, P=0.014), death/MI/CVA (13.7 *vs.* 28.8%, P=0.030) and repeat revascularization (8.6 *vs.* 28.9%, P=0.033).

Farooq, *et al.* [11] found that the RSS is an objective measure of the degree and complexity of residual stenosis after PCI. The RSS was > 0 to 4 in 20.4% [n=184], > 4 to 8 in 18.5% [n=167], and >8 in 16.9% [n=153]. It was seen that an RSS >8 was associated with significantly increased all-cause mortality (35.3%, P<0.001), MACCE (59.5%, P<0.001), MI (17.0%, P<0.001), all-cause revascularization (32.0%, P<0.001), and definite/probable stent thrombosis (16.0%, P=0.005) at 5 years follow up.

Conclusion

In patients of NSTE-ACS with MVD, complete revascularization either in the same setting or in a staged manner is better compared to only culprit vessel PCI in terms of long term total MACCE, cardiac death and the need for revascularization. There was no difference in MACCE outcomes between revascularization in the same setting and staged revascularization. In case of incomplete revascularization, RSS is a good and reliable predictor of total MACCE.

References

1. Murray CJ, Lopez AD (1997) Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. *Lancet* 349: 1498-504. [Crossref]

2. Yeh RW, Sidney S, Chandra M, Sorel M, Selby JV, et al. (2010) Population trends in the incidence and outcomes of acute myocardial infarction. *N Engl J Med* 362: 2155-2165. [Crossref]

3. Fox KA, Eagle KA, Gore JM, Steg PG, Anderson FA; GRACE and GRACE2 Investigators (2010) The Global Registry of Acute Coronary Events, 1999 to 2009--GRACE. *Heart* 96: 1095-1101. [Crossref]

4. Terkelsen CJ, Lassen JF, Nørgaard BL, Gerdes JC, Jensen T, et al. (2005) Mortality rates in patients with ST-elevation vs. non-ST-elevation acute myocardial infarction: observations from an unselected cohort. *Eur Heart J* 26: 18-26. [Crossref]

5. Task Force for Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of European Society of Cardiology, Bassand JP, Hamm CW, Ardissino D, Boersma E, et al. (2007) Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. *Eur Heart J* 28: 1598-1660. [Crossref]

6. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, et al. (2016) 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J* 37: 267-315. [Crossref]

7. Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, et al. (2014) 2014 AHA/ACC Guideline for the Management of Patients with Non–ST-Elevation Acute Coronary Syndromes. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 130: e344-e426. [Crossref]

8. Cannon CP, Weintraub WS, Demopoulos LA, Vicari R, Frey MJ, et al. (2001) Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. *N Engl J Med* 344: 1879-1887. [Crossref]

9. Fox KA, Poole-Wilson PA, Henderson RA, Clayton TC, Chamberlain DA, et al. (2002) Interventional versus conservative treatment for patients with unstable angina or non-ST-elevation myocardial infarction: the British Heart Foundation RITA 3 randomised trial. Randomized Intervention Trial of unstable Angina. *Lancet* 360: 743-751. [Crossref]

10. Wallentin L, Lagerqvist B, Husted S, Kontny F, Ståhle E, et al. (2000) Outcome at 1 year after an invasive compared with a non-invasive strategy in unstable coronary-artery disease: the FRISC II invasive randomised trial. *Lancet* 356: 9-16. [Crossref]

11. Farooq V, Serruys PW, Bourantas CV, Zhang Y, Muramatsu T, et al. (2013) Quantification of incomplete revascularization and its association with five-year mortality in the SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery (SYNTAX) trial validation of the RSS. *Circulation* 128: 141-151.

12. Généreux P, Palmerini T, Caixeta A, Rosner G, Green P, et al. (2012) Quantification and impact of untreated coronary artery disease after percutaneous coronary intervention: the residual SYNTAX (SYNergy between PCI with TAXus and cardiac surgery) score. *J Am Coll Cardiol* 59: 2165-2174. [Crossref]

13. Stefanini GG, Holmes DR Jr (2013) Drug-eluting coronary-artery stents. *N Engl J Med* 368: 254-265. [Crossref]

14. Head SJ, Kaul S, Mack MJ, Serruys PW, Taggart DP, et al. (2013) The rationale for Heart Team decision-making forpatients with stable, complex coronary artery disease. *Eur Heart J* 34: 2510-2518. [Crossref]

15. Farooq V, van Klaveren D, Steyerberg EW, Meliga E, Vergouwe Y, et al. (2013) Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percutaneous coronary intervention for individual patients: development and validation of SYNTAX score II. *Lancet* 381: 639-650. [Crossref]

16. Ben-Gal Y, Moses JW, Mehran R, Lansky AJ, Weisz G, et al. (2010) Surgical versus percutaneous revascularization for multivessel disease in patients with acute coronary syndromes: analysis from the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial. *JACC Cardiovasc Interv* 3: 1059-1067. [Crossref]

17. Palmerini T, Genereux P, Caixeta A, Cristea E, Lansky A, et al. (2011) Prognostic value of the SYNTAXscore in patients with acute coronary syndromes undergoing percutaneous coronaryintervention: analysis from the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial. *J Am Coll Cardiol* 57: 2389-2397. [Crossref]

18. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, et al. (2016) 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J* 37: 267-315. [Crossref]

19. Sardella G, Lucisano L, Garbo R, Pennacchi M, Cavallo E, et al. (2016) Single-Staged Compared With Multi-Staged PCI in Multivessel NSTEMI Patients The SMILE Trial. *J Am Coll Cardiol* 67: 264-272. [Crossref]

20. Bourassa MG, Yeh W, Holubkov R, Sopko G, Detre KM (1998) Long-term outcome of patients with incomplete vs complete revascularization after multivessel PTCA. A report from the NHLBI PTCA Registry. *Eur Heart J* 19: 103-111. [Crossref]

21. Tamburino C, Angiolillo DJ, Capranzano P, Dimopoulos K, La Manna A, et al. (2008) Complete versus incomplete revascularization in patients with multivessel disease undergoing percutaneous coronary intervention with drug-eluting stents. *Catheter Cardiovasc Interv* 72: 448-456. [Crossref]

22. Mariani G, De Servi S, Dellavalle A, Repetto S, Chierchia S, et al. (2001) Complete or incomplete percutaneous coronary revascularization in patients with unstable angina in stent era: Are early and one-year results different? *Catheter Cardiovasc Interv* 54: 448-453. [Crossref]

23. Shubrooks SJ, Malenka DJ, Piper WD, Bradley WA, Watkins MW, et al. (2000) Safety and efficacy of percutaneous coronary interventions performed immediately after diagnostic catheterization in northern new england and comparison with similar procedures performed later. *Am J Cardiol* 86: 41-45. [Crossref]

24. Hannan EL, Samadashvili Z, Walford G, Holmes DR, Jacobs A, et al. (2009) Predictors and Outcomes of Ad Hoc Versus Non-Ad Hoc Percutaneous Coronary Interventions. *JACC Cardiovasc Interv* 2: 350-356. [Crossref]

25. Jang JS, Jin HY, Seo JS, Yang TH, Kim DK, et al. (2015) Meta-analysis of multivessel versus culprit-only percutaneous coronary intervention in patients with non-ST-segment elevation acute coronary syndrome and multivessel coronary disease. *Am J Cardiol* 115: 1027-1032. [Crossref]

26. Ijsselmuiden AJ, Ezechiels J, Westendorp IC, Tijssen JG, Kiemeneij F, et al. (2004) Complete versus culprit vessel percutaneous coronary intervention in multivessel disease: A randomized comparison. *Am Heart J* 148: 467-474. [Crossref]

27. van den Brand MJ, Rensing BJ, Morel MA, Foley DP, de Valk V, et al. (2002) The effect of completeness of revascularization on event-free survival at one year in the ARTS trial. *J Am Coll Cardiol* 39: 559-564. [Crossref]

28. Nikolsky E, Gruberg L, Patil CV, Roguin A, Kapeliovich M, et al. (2004) Percutaneous coronary interventions in diabetic patients: is complete revascularization important?. *J Invasive Cardiol* 16: 102-106. [Crossref]

29. Yang HH, Chen Y, Gao CY (2010) The Influence of Complete Coronary Revascularization on Long-term Outcomes in Patients with Multivessel Coronary Heart Disease Undergoing Successful Percutaneous Coronary Intervention. *J Int Med Res* 38: 1106-1112. [Crossref]

30. Iqbal MB, Smith RD, Lane R, Patel N, Mattar W, et al. (2018) Prognostic significance of incomplete revascularization and bystander coronary anatomy following percutaneous coronary intervention: an observational study of 6,755 patients with multivessel disease. *Catheter Cardiovasc Interv* 91: 1229-1239. [Crossref]

31. Palmer ND, Causer JP, Ramsdale DR, Perry RA (2004) Effect of completeness of revascularization on clinical outcome in patients with multivessel disease presenting with unstable angina who undergo percutaneous coronary intervention. *J Invasive Cardiol* 16: 185-188. [Crossref]

32. Goldstein CL, Racz M, Hannan EL (2002) Impact of cardiac catheterization-percutaneous coronary intervention timing on inhospital mortality. *Am Heart J* 144: 561-567. [Crossref]

33. Witberg G, Lavi I, Assali A, Vaknin-Assa H, Lev E, et al. (2015) The incremental impact of RSS on long-term clinical outcomes in patients with multivessel coronary artery disease treated by percutaneous coronary interventions. *Catheter Cardiovasc Interv* 86: 3-10. [Crossref]