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Does Age of patient at influence Outcomes of PCI for Acute Coronary Syndrome? – Single-center Comparative Prospective Longitudinal Study

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Abstract

Objective:
The purpose of the study was to compare the presentation, intervention, and outcomes of ACS between the young and elderly population of India.
Method:
A hospital-based prospective longitudinal interventional case-control study was performed. The follow-ups of the patients were taken over six months (June 2018 to January 2019). The study involved the comparison of Risk factors, presentation, and outcomes at one month and six months was made between young (<65 years, n=140) and elderly patients (>65 years, n=140).
Results:
The demographics of both groups were comparable. Some major risk factors Demonstrated some disparity. Major risk factors which has higher incidence in elderly patients group included Unstable Angina (99.28% vs 87.85%), STEMI (65.71% vs 45%), Breathlessness (33.57% vs 9.28%) and heart failure (22.14% vs 10.71%), history of revascularization (11.42% vs 3.57%), hypertension(56.42% vs 43.57%), cerebral vascular accident(10% vs 2.85%), and anemia (40.71% vs 18.57%). The incidence of smoking history was significantly less in elderly patients vs. younger(36.42% vs. 22.14%). Most patients [186 (66.43%) total; (75.71% vs. 57.14%)] received were treated with coronary Angioplasty over medical therapy. However, more younger patients underwent angioplasty (75.71%) when compared to elderly patients (57.14%). At discharge, the incidence of MACE and other complications, viz. heart failure, bleeding, and renal dysfunction was higher in elderly vs. young patients. At six months, the incidence of heart failure was significantly higher in the elderly. After six months, the outcomes were similar. On stratified and ratio-balanced analysis, the outcome indicated that age is a stand-alone risk factor to affect the outcomes of angioplasty adversely.
Conclusion:
This study's outcomes indicated several limitations in performing angioplasty in the elderly population when compared with the younger population. The outcome of angioplasty, despite the selection of patients, is significantly worse in the elderly population.

Keywords*:*
Acute Coronary Syndrome, PCI in the elderly population, PCI, Percutaneous coronary intervention, STEMI, NSTEMI, Angioplasty, Coronary Stent, PAMI

I. Introduction

Acute coronary syndrome (ACS) is characterized by a sudden imbalance between myocardial oxygen consumption and demand, resulting in myocardial ischemia. The symptoms vary based on age, sex, and comorbidities[1]. Commonly, there is a disparity in ACS clinical presentations in the elderly[23](age > 65 years) compared with the younger population who commonly present with more atypical symptoms[456]. The differences in presentation, treatment, and outcomes of ACS between elderly and young patients were identified with the help of the study are commonly known. Hence, clinical differentiation is required in determining the diagnosis and treatment strategy, which needs to be dominantly age-based, considering that even sex-oriented variation of disease presentation tends to change with age.

While multiple physiological and metabolic changes could be a probable explanation of the influence of age in the ACS treatment, there are several unexplained areas, such as inequalities in the approach of therapy. These often remain as questions beyond pathophysiology and pharmacology of treatments for ACS. Hence, with increasing age, the patient's evaluation requires higher care towards therapy determination, mostly on an individualistic basis to control adverse incidents. The American Heart Association/American College of Cardiology (AHA/ACC) consensus guidelines[7]recommend reperfusion in all eligible patients. However, in the real world, often, the comorbidities limit the scope of angioplasty in older age patients[89].

While several studies have evaluated and established the influence of age on worsening outcomes of Angioplasty

in ACS, there is limited evidence to support similar outcomes in the Indian population. The data mainly originates from Europe and North America. Hence, the populational differences in terms of its demographics. Considering differences in weather and environment, food habits, exercise, gender ratio, lifestyle, etc., several predisposing factors are grossly unvalidated while evaluating the effect of age on angioplasty outcomes with Elderly defined as age > 65 years as per World Health Organization (WHO) definition[10]. Hence, this study was an effort to signify and validate the population outcomes in the Indian context. However, a mere collection of data and analysis would not generate value beyond anecdotal opinion. Hence, this study was designed to be a prospective longitudinal study.

II. Methodology

This study was designed to include real-world Acute Coronary Syndrome patients. The sample size was statistically calculated as 140 subjects in each arm with an F-test (10.9% margin of error, 50% as response distribution, and 99% confidence interval (CI)). Systematic sampling was used for selecting every alternate ACS patient in both the elderly and control groups. The enrollment was terminated in both the groups once the predetermined sample size of 140 subjects was reached. Approval from the Institutional Ethics committee was obtained before the study.

All the patients who were diagnosed for ACS in the period of 6 months (June 2018 to January 2019) were approached and enrolled in the study after obtaining formal written informed consent following medical counseling of patients and relatives regarding medical vs. invasive PCI/Coronary artery bypass grafting (CABG)] treatment as indicated. All Subjects were screened with Electrocardiogram (ECG) and the 2D Echo, haemogram for Anaemia[11], and glomerular filtration rate (GFR). As per the practice norms, the patients were classified into STEMI/NSTEMI based on clinical history, ECG, and cardiac enzymes. Of these patients admitted for elective coronary angiogram/ percutaneous coronary intervention (PCI), end-stage disease and significant comorbidities having a life expectancy of <6 months were excluded from the study.

The subjects were treated as per the standard treatment protocol of the hospital. The study had no role in determining treatment choice. Data related to clinical presentation, past medical history, and risk factors were collected at the baseline. The assessment of all parameters viz. clinical cardiac assessment, ECG, GFR, Hb, and the 2D echo was performed at baseline and at one month and six months follow-up to identify any major adverse cardiac and events (MACE), significant bleeding, cerebrovascular accident, renal dysfunction, or heart failure. The MACE was defined as a composite endpoint of cardiac death, non-fatal MI, and repeat revascularization. Heart failure was considered as per with European Society of Cardiology 2016 guidelines[12]. Renal dysfunction was defined as GFR <60 ml/min/1.732 by Cockcroft and Gault formula as per KDIGO guidelines[13].

The analysis was performed with MS Excel, Minitab Software, and SAS, as applicable. The study's primary outcome measure was set to be all-cause mortality at one month after revascularization. All-cause mortality at six months was the major secondary outcome measure.
Demographics, clinical presentation, and laboratory parameters were considered as other primary explanatory variables, with age being the primary variable for define case vs. control.
Descriptive analysis was performed using mean and standard deviation for quantitative variables, frequency, and proportion for categorical variables. Abnormally distributed quantitative variables were summarized by the median and interquartile range (IQR). For customarily distributed quantitative parameters, the mean values were compared between study groups using an independent sample t-test. All quantitative variables were checked for normal distribution with each category of the explanatory variable using visual inspection of histogram and normality Q-Q plots. The Shapiro-Wilk test was also conducted to assess the normal distribution, and the p-value >0.05 was considered normal distribution. Categorical outcomes were compared between study groups using the Chi-square test/Fisher's extract test (if the overall sample size was <20 or if the expected number in any of the cells is <5, Fisher's extract test was used). A P-value of <0.05 was considered statistically significant.

III. Results

Demographics and Baseline characteristics

In all,280 patients, with 140 each group, were included in the study, distributed as 69 females and 211 males (male: female ratio –3.06). The control group (age < 65 years) had 120 males and 20 females (male: female ratio – 0.16) in the case group (>65 years) had 91 males and 49 females (male: female ratio 1.8) in the case group. The overall mean age was in the control group was 52.66 ± 8.15 years, and in the case group was 71.89 ± 6.3 years ($p<0.05$) (table 1).

Table 1 Age Distribution of the cohort

Parameter	Total sample			Gender wise data					
	<65 yrs (control)	>65 yrs (case)	p-value	<65years (control)			>65 years (case)		
				Male	Female	p-value	Male	Female	
Total patients (n)	140	140	-	120	20	-	91	49	-
Age (mean ±SD)	52.66 ± 8.15	71.89 ± 6.3	<0.05	52.46 ± 8.05	53.85 ± 8.8	>0.05	71.56± 6.68	72.49 ± 5.54	>0.05

As compared the control group, significantly more (p<0.05) patients in the case group had breathlessness (9.28% vs 33.57%) and anaemia [40.71% (n=57) vs 18.57% (n=26)] was significantly more common in case vs control group (p<0.05). History of smoking was significantly more common in control vs case group [36.42% (n=51) vs 22.14% (n=31), p<0.05]. Palpitation was marginally higher in case group (7.14% vs 12.85%) and altered sensorium was equal (1.42% vs 1.42%) with low statisticalsignificance (Table 2).

Significant difference was observed between history of revascularization [11.42% (n=16) vs 3.57% (n=5)], hypertension [56.42% (n=79) vs 43.57% (n=61)], cerebral vascular accident [10% (n=14) vs 2.85% (n=4)] and heart failure (10.71% vs 22.14%). History of dyslipidemia [27.85% (n=39) vs 19.28% (n=27)] and peripheral vascular disease [1.42% (n=2) vs 2.14% (n=3)] were not significantly different between the groups (p>0.05) (table 2).

The Incidence of UA was higher in the control (99.28%) group as compared with the case group (87.85%) (p<0.05). STEMI was significantly more common in control vs. case group [65.71% (n=92) vs 45% (n=63), p<0.05)]. NSTEMI was more common in case vs control group [55% (n=77) vs 34.3% (n=48), p<0.05]. Posterior wall MI was significantly more common in control vs case group [14.3% (n=20) vs 6.4% (n=9), p<0.05]. Incidences of anterior wall [31.42% (n=44) vs 21.42% (n=30)], inferior wall [31.42% (n=44) vs 21.42% (n=30)] and lateral wall MI [4.3% (n=6) vs 2.9% (n=4)] did not differ significantly (p>0.05) between the groups (table 2).

Heart failure was significantly more common in case [22.14% (n=31)] vs control group [10.71% (n=15)] (p<0.05). Valvular dysfunction was also more common in case [17.1% (n=24)] vs control group [2.1% (n=3)]. There was no significant difference (p>0.05) between the control vs case groups: regional wall motion abnormalities [67.1% (n=94) vs 67.1% (n=94)], diastolic dysfunction [32.1% (n=45) vs 35% (n=49)], left ventricular clot [1.4% (n=2) vs 0.7% (n=1)] and pericardial effusion [0.7% (n=1) vs 2.9% (n=4) (table 2).

Table 2 Clinical presentation, risk factors, EEG findings, 2D echo findings and

Table 2: Clinical presentation, risk factors, EEG findings, 2D echo findings

Parameter	Age		p-value
	<65 year (n=140)	>65 years (n=140)	
Clinical presentation			
Angina	139 (99.28%)	123 (87.85%)	<0.001
Breathlessness	13 (9.28%)	47 (33.57%)	<0.001
Palpitation	10 (7.14%)	18 (12.85%)	0.111
Heart failure	15 (10.71%)	31 (22.14%)	0.01
Altered sensorium	2 (1.48%)	2 (1.42%)	1.00
Risk factors			
History of revascularization	5 (3.57%)	16 (11.42%)	0.013
Diabetes mellitus	78 (55.71%)	78 (55.71%)	1.000
Hypertension	61 (43.57%)	79 (56.42%)	0.031
Dyslipidemia	39 (27.85%)	27 (19.28%)	0.091

Peripheral vascular disease	**2 (1.42%)**	**3 (2.14%)**	**0.652**
Smoking	51 (36.42%)	31 (22.14%)	0.009
History of cerebrovascular disease	4 (2.85%)	14 (10%)	0.015
Anaemia	26 (18.57%)	57 (40.71%)	<0.001
ECG presentation - STEMI			
Anterior wall MI	44 (31.42%)	30 (21.42%)	0.058
Inferior wall MI	44 (31.42%)	30 (21.42%)	0.058
Lateral wall MI	6 (4.3%)	4 (2.9%)	0.520
Posterior wall MI	20 (14.30%)	9 (6.4%)	0.031
Overall STEMI	92 (65.71%)	63 (45%)	<0.001
ECG presentation - NSTEMI			
NSTEMI	48 (34.3%)	77 (55%)	<0.001
2D echo findings			
Regional wall abnormalities	94 (67.1%)	94 (67.1%)	1.0
Diastolic dysfunction	45 (32.1%)	49 (35%)	0.613
Left ventricular clot	2 (1.4%)	1 (0.7%)	0.562
Pericardial effusion	1 (0.7%)	4 (2.9%)	0.176
Ventricular septal rupture	0 (0%)	0 (0%)	-
HF with EF <40%	15 (10.71%)	31 (22.14%)	0.010
Valvular dysfunction	3 (2.1%)	24 (17.1%)	<0.001

STEMI: ST-elevation myocardial infarction; NSTEMI: Non-ST elevation myocardial infarction; MI: Myocardial infarction; ECG: Electrocardiogram; HF: Heart failure; EF: Ejection fraction

Out of 140 in the control arm, 106 (75.71%) underwent revascularization, while in the case arm, 80 (57.14%) could be treated with revascularization. Forty-four (31.42%) patients in the control arm and 61(43.57%) were treated with conservative therapy ($p<0.05$) (table 3). The Revascularization: Conservative therapy ratio of control vs. case group was 2.41 vs. 1.33.

Medical treatment was administered to and in the control and case group, respectively.

Table 3 treatment administered in control and case groups.

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Parameter	**Age**		**p**
	<65 year (n=140)	>65years (n=140)	
Conservative / Medical	44 (31.42 %)	61 (43.57 %)	0.036
Revascularization/invasive	106 (75.71 %)	80 (57.14 %)	0.001
Conservative: Revascularization Ratio	2.41	1.33	N/A

During the hospital stay, the incidence of heart failure was in the case group was 26.4% (n=37) was compared with 10.7% (n=15) in the control group. Bleeding events occurred in 8 (5.7%) and 1 (0.7%) and renal dysfunction occurred in 24 (17.1%) and 13 (9.3%) patients in case group and control groups respectively ($p<0.05$). There was no evidence of cerebral vascular accidents. In the control group, 2 (1.4%) patients had stent thrombosis. In the case group, 1 (0.7%) patient had re-infarction (table 2).

At one month, there was no significant difference in outcomes between the two age groups ($p>0.05$), except for heart failure, which was significantly more common in the case group [16.3% (n=22)] vs. control group [7.2% (n=10)] ($p<0.05$). In both the group, there was no incidence of cardiac deaths,

cerebrovascular accidents, stent thrombosis, and bleeding. In the control group, 1 (0.7%) patient had non-fatal MI, and 9 (6.5%) patients had renal dysfunction. In the case group, 2 (1.5%) patients had non-fatal MI, and 15 (11.1%) patients had renal dysfunction (table 5).In addition, there was an analysis of all-cause mortality and MACE at six months. There was one (0.71%) death in the control group during hospitalization; the patient had received revascularization. In the case group, there were 5 (3.57%) deaths (p>0.05) [3 (60%) had received conservative medical therapy and 2 (40%) revascularizations (table 4)].

Table 4 Comparison of mortality between the two groups

Table 4: Comparison of mortality between the two groups			
	Age group		p
	< 65 years (n=140)	> 65 years (n=140)	
Overall	1 (0.71%)	5 (3.57%)	>
mortality			0.05
Mortality in treatment groups			
Conservative / medical	0 (0%)	(60%)	-
Revascularization/invasive	1 (0.71%)	(40%)	-

Patients who died were excluded from the analysis. Hence, 139 patients and 135 patients were included from the control and case groups, respectively.

The outcomes did not differ significantly between the 2 groups at six months. In the control group, one (0.7%) patient had cardiac death; one had a cerebral vascular accident (0.7%), and9 (6.5%) had renal dysfunction; non-fatal MI, stent thrombosis, and bleeding were not reported. In the case group, 1 (0.7%) patient had non-fatal MI, 1 (0.7%) had to bleed, and 16 (11.9%) had renal dysfunction; cardiac death, cerebrovascular accident, and stent thrombosis were not reported (Table 5).

Table 5 Comparison of outcomes at 1-month and six months post-acute coronary syndrome between two groups

Table 5: Comparison of outcomes at 1-month and six months post-acute coronary syndrome between two groups						
Outcomes	One month			Six months		
	Age group		p-value			p-value
	<65 yrs (n=139)	>65 yrs (n=135)		<65 yrs (n=139)	>65 yrs (n=135)	
Cardiac death	0 (0%)	0 (0%)	-	1 (0.7%)	0 (0%)	-
Non-fatal myocardial infarction	1 (0.7%)	2 (1.5%)	>0.05	0 (0%)	1 (0.7%)	-
Cerebrovascular accident	0 (0%)	0 (0%)	-	1 (0.7%)	0 (0%)	-
Heart failure	10 (7.2%)	22 (16.3%)	<0.05	10 (7.2%)	18 (13.3%)	>0.05
Stent thrombosis	0 (0%)	0 (0%)	-	0 (0%)	0 (0%)	-
Bleeding	0 (0%)	0 (0%)	-	0 (0%)	1 (0.7%)	-
Renal dysfunction	9 (6.5%)	15 (11.1%)	>0.05	9 (6.5%)	16 (11.9%)	>0.05

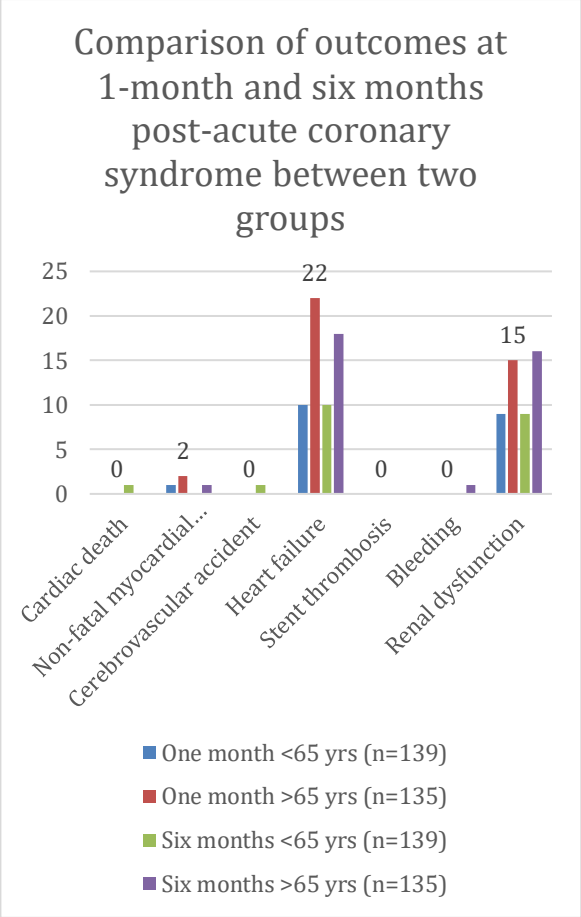

Figure 1Comparison of outcomes at 1-month and six months post-acute coronary syndrome between two groups

Discussion

Coronary artery disease (CAD) is becoming more familiar with increasing life expectancy. The Elderly now constitute a significant portion of the world population. Thus, there is a need for more attention to the understanding of CAD among the elderly. Atypical presentations were more common among the elderly in this study. Anginawaspresent in almost all young patients (99.28%) when compared to the elderly (87.85%) ($p<0.05$). It is known that elderly patients have an increased pain threshold of permanently ischemic sensory nerves, ischemic dysfunction of the cerebral cortex, and the autonomic nervous system; these could be the reasons for the lower prevalence of angina in the elderly[14]. Chaugh A et al.[15] and Woon VC et al.[4] also reported a higher prevalence of angina among the younger population vs. the older population. Breathlessness was significantly more common among the elderly (33.57%) vs. young patients (9.28%) ($p<0.05$) in this study. Chaugh A et al. [15] Bhatia et al.[16] also reported similar observations. Holay MP et al.[17] reported a significantly higher prevalence of palpitation as well among the elderly when compared to young patients ($p<0.05$). Except for smoking, the risk factors did not differ significantly between young and elderly patients in this group (36.42% in young vs. 22.14% in old, $p<0.05$). Perhaps, with aging, most people quit smoking. Diabetes and hypertension, along with dyslipidemia, is perhaps a risk factor for heart disease in both populations but more so among the younger population. Several previous studies reported similar observations.[4,15,16,17]. With respect to ECG findings, STEMI was significantly more commonly reported in the elderly (65.7%) when compared to the younger population (45%) ($p<0.05$) in this study, the results were in agreement with previous studies [16,18]. However, a study by Chaugh A et al.[15] had reported a similar incidence of STEMI or NSTEMI among young and elderly patients.

In this study, much lesser elderly ACS patients received revascularization (57.14%) when compared to young patients (75.71%, $p<0.05$). The observations of this study also suggest inequalities in the treatment of the elderly, which were in line with studies by Tresch DD et al.[19]and Mehta RH et al.[20]The inequality could be because of comorbidities and the perception of being at high risk. Like earlier studies [15, 16, 17], complications such as heart failure, renal dysfunction, and bleeding during hospital stay were common among elderly vs. younger patients in this study. Since cardiac failure is an indicator of poor ACS[21] in the elderly, strategies to prevent and treat cardiac failure in the elderly are essential. Mortality was higher among the elderly (3.5%, five deaths) than young (0.71%, one death). A higher incidence of comorbidities could be the reason for higher mortality in the elderly. The mortality rate in this study group was low in comparison to other studies [16, 17]. This could be explained by us being a tertiary care cardiac unit; patients may have received prompt treatment. At one-month and six-month follow-ups, heart failure was significantly more common ($p<0.05$) among the elderly vs. younger population in this study, which was in agreement with Holey MP et al.[17]study. In this study, complications were less frequent at six months follow-up. They did not differ significantly between age groups.

Post-hoc propensity matching base quasi-equated analysis for the data was performed with the RADHIKa method[22]. All the risk factors were used as the predictors of risk, and a standardized ratio (mean = value, focused mean = 0.05 and SD=1) was calculated. The average of all these ratios, called RADHIKa factor (ψ), was observed as 0.969, revealing that the two groups had a marginal similarity. This score was used to calculate the predicted value for outcomes in the group with age >65 by multiplying values in the group with age <65. For population-standard ratio (RADHIKa) values, the standardized ratio of both groups was multiplied by ψ. The Range was calculated using normal confidence interval with mean asRADHIKa values and Standard Deviation of the case and control. A stock graph was plotted for these four values, revealing that despite an almost similar population, age is a standalone risk factor for all major complications of ACS, especially Heart Failure and Renal Dysfunction, and MI (MI in the shorter term) (Figure 2,3).

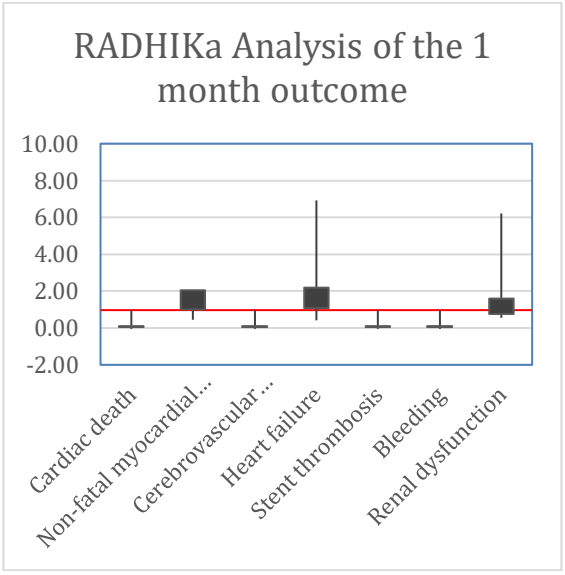

Figure 2: RADHIKa Analysis at 1 month

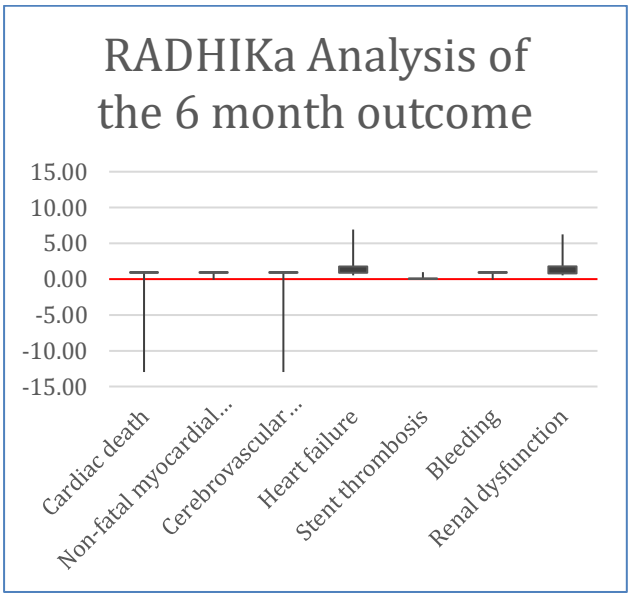

Figure 3: RADHIKa Analysis at 6 months

The main limitation of this study was the small sample size. Also, appropriate and timely treatment intervention could not be done in some instances due to patients' financial constraints. This may have affected the immediate and long-term outcomes in these patients.

IV. Conclusion

This study showed differences in presentation, treatment choice, and outcomes between the elderly and young. Considering these differences could improve the treatment and outcomes. There is also a need to eliminate the inequalities in treatment, especially revascularization, between age groups. Further large-scale studies are required to shed more light on the age and gender differences such that treatment can be optimized.

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