

# Comparison of demographic profile, risk factors, and in-hospital outcome in young and old patients with acute coronary syndrome: A single-center experience

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## ABSTRACT

**Background:** Coronary artery disease (CAD) is witnessing a demographic transition with increasing prevalence in younger individuals. Data is scarce comparing various characteristics of acute coronary syndrome (ACS) between young and old patients in an Indian setting. Hence, we evaluated the epidemiological, demographic, risk factor, and outcome profile of young and old ACS patients in Indian setting. **Methods:** This was a prospective observational study, which enrolled 50 consecutive ACS patients each into two groups: younger ( $\leq 45$  years) and elderly ( $> 45$  years), respectively. Comparison of clinical presentation, electrocardiography, echocardiographic findings, conventional, nonconventional risk factors, and in-hospital outcomes including duration of hospital stay and major adverse cardiac events (MACE) were made between the two groups. Multivariate regression analysis of risk factors as determinants of MACE adjusting for other confounding factors was also performed. **Results:** Fifty patients in each group were compared. Mean age in the younger and elderly group was  $36 \pm 4.69$  and  $61.58 \pm 10.69$  years, respectively. Male sex, smoking, family history of CAD, hyperhomocysteinemia, and obesity were observed more in the younger population. While dyslipidemia, low physical activity, diabetes mellitus, and history of previous ACS was more in the older population. Single-vessel disease was more common in younger patients while multivessel involvement was more common in elderly patients. Older patients had longer hospital stays and more in-hospital MACE including deaths. By multivariate analysis, shock was found to be an independent predictor of MACE in both groups. **Conclusion:** Younger ACS patients have a different risk profile and better in-hospital outcomes compared to older patients.

**Keywords:** Acute coronary syndrome, major adverse cardiac events, risk factors, stroke

## Introduction

The contribution of coronary artery disease (CAD) to cardiovascular disease burden is increasing in India.<sup>[1,2]</sup> Acute coronary syndrome (ACS), which includes unstable angina,

non-ST elevation myocardial infarction (NSTEMI), and ST elevation myocardial infarction (STEMI) is the major cause of mortality in CAD.<sup>[3]</sup> Compared with people of European ancestry and western population, CAD occurs a decade earlier in Indians.<sup>[3,4]</sup>

Recently, the frequency of acute myocardial infarction has been increased in the younger population.<sup>[4]</sup> Young patients ( $< 40$  years) with ACS had a high prevalence of smoking, family history of CAD, dyslipidemia, myocardial infarction with normal coronary

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arteries (MINOCA), and single-vessel disease (SVD).<sup>[5,6]</sup> Several risk factors of ACS have been reported; however, their role in the pathogenesis of ischemic heart disease and their importance in determining the clinical outcomes among young patients is still not convincingly established. Thus, the present study was designed to elucidate these lacunae in the demographic and risk profile of the younger ACS patients.

## Material and Methods

This was a prospective, cross-sectional observational study conducted at a tertiary hospital of North India between January 2016 and May 2017. The study enrolled 50 consecutive patients with ACS, fulfilling the inclusion criteria, each into young (<45 years) and old ( $\geq 45$  years) groups, respectively. The study strictly followed the standard clinical guidelines and institutional ethics committee has approved the study. Written informed consent was obtained from all patients or their guardians prior to enrollment.

Patients with an age  $\geq 18$  years, unstable angina: STEMI and NSTEMI were included in the study. However, patients who had already undergone revascularization by percutaneous or surgical [percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG)] or had developed stent thrombosis were excluded.

### Definitions and data collection

Patients of unstable angina, NSTEMI, and STEMI were diagnosed based on previously established standard definitions.<sup>[7,8]</sup>

Chest pain was recorded either as typical angina, atypical angina, or nonanginal chest pain.<sup>[9]</sup> Details of risk factors including age, gender, and family history of premature CAD (first-degree relatives with males <55 years and females <65 years) were noted. History of diabetes, hypertension, and other comorbidities in both groups were recorded. Anthropological data including body mass index (BMI) and waist circumference were recorded and categorized based on Asian standards and definitions.<sup>[10]</sup>

Smoking history was also taken from all patients. Active smokers were defined as those who reported smoking at least 100 cigarettes in their lifetime and who, at the time of study, smoked either every day or some days. Ex-smokers as those who quit 30 days before enrollment and never smokers as those who had smoked less than 100 cigarettes in their lifetime. Self-reported physical activity data was collected using the international physical activity questionnaire form and based on these patients were divided into low, moderate, and high level of activity.<sup>[11,12]</sup>

Complete lipid profile was examined, and patients were classified as having dyslipidemia if they have represented low-density lipoprotein (LDL) >100 mg/dL, high density lipoprotein (HDL) <40 mg/dL in males and <50 mg/dL in females, triglycerides >150 mg/dL, or total cholesterol >200 mg/dL.<sup>[13]</sup> Clinical chemistry analyzer based on particle-enhanced turbid metric

immunoassay method was used to estimate high-sensitive C-reactive protein (hs-CRP) levels in serum. Plasma homocysteine levels were measured using chemiluminescence immunoassay method, and apolipoprotein-A1 was analyzed based on nephelometry.

All patients were followed up during hospital stay and in-hospital outcomes were noted. Pharmacotherapy in the form of aspirin, P2Y12 inhibitors (clopidogrel), statins, angiotensin converting enzyme inhibitor/angiotensin receptor blocker, beta-blockers, or novel antianginal drugs were given to all the patients. Major adverse cardiovascular events (MACE), including deaths, reinfarction, stroke, resuscitated cardiac arrest, and major bleeding were also determined during admission and at follow-up.

### Statistical analysis

Mean or median was used for quantitative variables and frequencies or proportions for qualitative variables. Comparison between groups was done using Chi-square test for qualitative variables and independent t test or Mann Whitney U test for quantitative variables. Multivariate analysis was done to find independent predictors of MACE. All tests were two-tailed, and  $P$  value < 0.05 was considered as significant. Statistical analysis was done using SPSS 22 version.

## Results

The mean age of patients in the younger group was  $36 \pm 4.69$  years and in the elderly group was  $61.58 \pm 10.69$  years. The percentage of females in the elderly group was almost double than that of younger group (33.3% vs 18.8%). A comparison of complete baseline and clinical profile of both groups is depicted in Table 1.

In the elderly group, STEMI was found in 62.5%. However, in the younger group NSTEMI and unstable angina were more common (58.4%). Majority of patients presented with typical angina pain (83.3% in elderly group vs 68.8% in the younger group). Dyspnea and palpitations were more common in the elderly group. Furthermore, sympathetic over activity manifested as tachypnea, tachycardia, and sweating were more prevalent in the older age group. Among all, 79.2% younger patients presented with Killip class-1, while 58.3% of the elderly group had Killip class-1, and the remaining 41.7% of elderly belonged to Killip class  $\geq 2$ . More number of elderly patients (6) than younger patients (1) developed cardiogenic shock (Killip class 4). Two patients from the elderly group reported a murmur of mitral regurgitation on examination.

More number of elderly patients were diabetic (20.8% vs 41.7%,  $P = 0.009$ ). Four patients in each group had a history of a prior stroke. Low level of physical activity was significantly prevalent in the elderly patients. Arrhythmias were also of higher prevalence in the older age group. Left ventricular systolic function was preserved (ejection fraction >55%) in a higher proportion in younger patients compared to the elderly group (27 vs 21 patients,  $P = 0.031$ ). Severe left ventricular systolic dysfunction (9 vs 1 patients) and mitral regurgitation was higher in the older patients (5 vs 2 patients).

**Table 1: Baseline demographic characteristics**

Variables	Young (≤45 years) (n=48)	Old (>45 years) (n=48)	P
Age, years (mean±SD)	36.23±4.69	61.58±10.69	0.001
Gender, n (%)			
Male	39 (81.3)	32 (66.7)	0.162
Female	9 (18.8)	16 (33.3)	
Risk Factors, n (%)			
Diabetes mellitus	10 (20.8)	22 (45.8)	0.009
Hypertension	18 (37.5)	22 (45.8)	0.408
Current smoker	31 (64.6)	16 (33.3)	0.011
Ex-smoker	3 (6.3)	5 (10.4)	
Cerebrovascular accident	4 (8.3)	4 (8.3)	1.000
Family history of CAD	15 (31.3)	10 (20.8)	0.245
History of previous MI	3 (6.3)	7 (14.6)	0.181
Menopause	1 (11.1)	15 (93.8)	0.005
Physical Activity, n (%)			
Low	13 (27.1%)	20 (41.7%)	0.118
Moderate	28 (58.3%)	26 (54.2%)	
High	7 (14.6%)	2 (4.2%)	
Body Mass Index, kg/m <sup>2</sup>	24.76±3.25	24.33±3.03	0.507
Underweight, n (%)	1 (2.1)	1 (2.1)	0.879
Normal, n (%)	15 (31.3)	15 (31.3)	
Overweight, n (%)	21 (43.8)	24 (50)	
Obese, n (%)	11 (22.9)	8 (16.7)	
Waist Circumference	86.75±8.81	91.16±8.95	0.017
Clinical Symptoms			
Chest pain			
Angina	33 (68.8)	40 (83.3)	0.132
Atypical angina	13 (27.1)	8 (16.7)	
Dyspnea	10 (20.8)	19 (39.6)	0.045
Paroxysmal nocturnal dyspnea	4 (8.3)	7 (14.6)	0.336
Orthopnea	3 (6.3)	12 (25)	0.011
Shock	4 (8.3)	7 (14.6)	0.336

CAD: coronary artery disease; MI: myocardial infarction

Total cholesterol ( $209.82 \pm 35.47$  vs  $197.96 \pm 43.57$ ,  $P = 0.147$ ), low-density lipoprotein (LDL) ( $162.03 \pm 31.21$  vs  $141.53 \pm 40.27$ ,  $P = 0.006$ ), triglyceride ( $192.32 \pm 34.78$  vs  $177.19 \pm 52.92$ ,  $P = 0.10$ ), and high-sensitivity C-reactive Protein (hs-CRP) levels ( $39.16 \pm 29.21$  vs  $29.52 \pm 30.42$ ,  $P = 0.11$ ) were numerically higher in the elderly group. On the other hand, the younger group had higher levels of high-density lipoprotein (HDL) ( $42.48 \pm 12.81$  vs  $40.99 \pm 12.23$ ,  $P = 0.56$ ), homocysteine ( $16.23 \pm 12.42$  vs  $13.86 \pm 7.00$ ,  $P = 0.25$ ), and apolipoprotein A1 ( $125.44 \pm 39.25$  vs  $122.74 \pm 30.09$ ,  $P = 0.706$ ). One patient in each group was taken up for coronary artery bypass graft (CABG). Thrombolysis was done in a higher proportion of the older patients (27.1% vs 22.9%,  $P = 0.63$ ). Coronary angiography was done in all patients, while percutaneous coronary intervention (PCI) was carried out in a higher number of younger patients compared to the older subjects (79.2% vs 70.8%,  $P = 0.346$ ). Clinical findings and procedural characteristics were shown in Table 2.

The incidence of MACE was reported in 17 (35.4%) elderly patients and 5 (10.4%) younger patients. The incidences of arrhythmias (6.3% vs 2.1%,  $P = 0.61$ ), cardiac arrest (10.4% vs 4.2%,  $P = 0.435$ ), and in-hospital myocardial infarction (2.1%

in older group and none in younger group) were numerically higher in the older age group. The management and clinical outcomes are depicted in both the groups are depicted in Table 3. A univariate analysis represented a significant association of MACE with shock, dyslipidemia, hs-CRP levels, and significant CAD on angiography [Table 4]. Furthermore, multivariate logistic regression analysis of significant univariate variables with that of MACE showed shock to be a significant variable in determining MACE [Table 5].

## Discussion

India as a developing nation has witnessed major transitions in all spheres. One arena of change relevant to us has been the change in demographic patterns of certain diseases.<sup>[1,4]</sup> Widespread globalization and alteration in socio-economic factors have altered the epidemiology of major noncommunicable diseases as well. Recently, CAD has grown to epidemic proportions, and there has been a demographic shift of the ACS spectrum in younger populations.<sup>[3,4]</sup>

In this comparative cross-sectional study between young and old ACS patients, we found STEMI as common in the older patient

**Table 2: Clinical findings and procedural characteristics**

Variables	Young (≤45 years) (n=48)	Old (>45 years) (n=48)	P
Clinical Presentation, n (%)			
STEMI	20 (41.7)	30 (62.5)	0.086
NSTEMI	13 (27.1)	6 (12.5)	
Unstable Angina	15 (31.3)	12 (25)	
Lipid Profile, mg/dL (mean±SD)			
Total cholesterol	197.96±43.57	209.82±35.47	0.147
Low density lipoprotein	141.53±40.27	162.03±31.21	0.006
High density lipoprotein	42.48±12.81	40.99±12.23	0.562
Triglycerides	177.19±52.91	192.32±34.78	0.101
Apolipoprotein A1	125.44±39.25	122.74±30.09	0.706
Homocysteine	16.23±12.42	13.86±7.00	0.253
High-sensitive C-reactive protein	29.52±30.42	39.16±29.21	0.117
Angiographic Findings, n (%)			
Significant CAD	40 (83.3)	41 (85.4)	0.779
Culprit Vessel			
Left main coronary disease	00	1 (2.1)	--
Left circumflex artery	22 (45.8)	22 (45.8)	--
Right coronary artery	20 (41.7)	23 (47.9)	0.538
Left anterior descending	27 (56.3)	29 (60.4)	0.679
Number of Vessel Involved			
Single vessel disease	19 (39.6)	13 (27.1)	0.527
Double vessel disease	16 (33.3)	22 (45.8)	
Triple vessel disease	7 (14.6)	6 (12.5)	
None	6 (12.5)	7 (14.6)	

CAD: coronary artery disease

**Table 3: Management and in-hospital major adverse cardiac events**

Variables	Young (≤45 years) (n=48)	Old (>45 years) (n=48)	P
Pharmacotherapy	48 (100%)	48 (100%)	-
Thrombolysis	11 (22.9%)	13 (27.1%)	0.637
Streptokinase	9 (18.7%)	12 (25%)	
Retepase	2 (4.2%)	1 (2.1%)	
CABG	1 (2.1%)	1 (2.1%)	-
PCI	38 (79.2%)	34 (70.8%)	0.346
Death	1 (2.1%)	4 (8.3%)	0.362
In-hospital MI	00	1 (2.1%)	1.000
Stroke	00	1 (2.1%)	1.000
Bleeding	1 (2.1%)	3 (6.3%)	0.617
Cardiac arrest	2 (4.2%)	5 (10.4%)	0.435
Arrhythmias	1 (2.1%)	3 (6.3%)	0.617

CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention; MI: myocardial infarction

while NSTEMI and unstable angina were more prevalent in the younger patients. Diabetes mellitus, hypertension, dyslipidemia, and ex-smoking were more prevalent in the elderly group. While current smoking, family history of premature CAD, and hyper homocystinemia were more common in the younger group. Single-vessel involvement on angiography was more prevalent in the younger population while multi-vessel involvement was more common in the older population. MACE including in-hospital mortality was higher in the older population, and shock was found to be an independent predictor of the same during hospital stay.

In our study, mean age of young and elderly patients was (36.23 ± 4.69 years vs. 61.58 ± 10.69 years) with 1/3<sup>rd</sup> being male population in both groups. These findings were similar to majority of all previous studies including the national registry of myocardial infarction (NRFMI), which showed the ACS frequency in older group to be double than that in the younger age group (32.3 vs 16%).<sup>[14]</sup> STEMI was more frequent in elderly patients than younger patients (62.5% vs 41.7%). NSTEMI and unstable angina were more frequent in the younger population. These results were supported by the observations of Avezum *et al.* from the Global Registry of Acute Coronary Events (GRACE).<sup>[15]</sup> In the Kerala registry, STEMI was found in 37%, NSTEMI in 31%, and unstable angina in 32% of the patients.<sup>[16]</sup> While in the HP ACS registry, NSTEMI and unstable angina (54.5%) outnumbered the number of STEMI cases (45.5%).<sup>[17]</sup> This difference could be attributed to multitude of factors ranging from berkesonian bias, sample size, population genetics, difference in risk factors, and heterogeneity of presentation of ACS spectrum.

Another most common risk factor is the lifestyle and physical activity status of the individual. In our study, we found that majority of patient had moderate levels of physical activity as calculated by the International Physical Activity Questionnaires (IPAQ) scoring system (58.3% in the younger group and 54.2% in the older group). Sedentary lifestyle/low-level activity was more prevalent in the elderly group (41.7% vs 27.1%). These findings were discordant with a study by Marcus *et al.* where sedentary behavior was found as a significant risk factor in younger individuals as well.<sup>[18]</sup> The difference in these results could be attributed to different methods of measuring physical activity, different population with different socio-demographic features, and difference in sample size. Prevalence of diabetes was higher in the older group (45.8% vs 20.8%).

We found the mean levels of cholesterol, LDL, triglycerides, and hs-CRP were significantly higher in the elderly population while HDL levels in elderly was comparatively lower. Similarly, Obaya *et al.* found dyslipidemia to be the most common risk factor for the elderly (96.8%) patients.<sup>[19]</sup> This was, however, discordant with Avezum *et al.* of the GRACE registry, which stated that dyslipidemia in the elderly patients was 35%.<sup>[15]</sup> In our study, homocysteine levels were higher in the younger group. F Martín-Herrero *et al.* found that high levels of homocysteine were strong predictors of cardiac events in young patients with ACS.<sup>[20]</sup>

Single-vessel involvement was more common in the younger group (39.6% vs 27.1%) while double-vessel involvement was more common in the elderly group (45.8% vs 33.3%). Similarly, Zimmermann *et al.* also found single-vessel involvement to be more common in the younger group while multi-vessel in the elderly population.<sup>[5]</sup>

Thrombolytic therapy was given to 27.1% and 22.9% in the older and younger age group, respectively. We found PCI rates were higher in the younger population (79.2% vs 70.8%), which was in line with previous studies.<sup>[19,21,22]</sup> We found shorter hospital stays and better clinical outcomes in younger patients. The presence of



**Table 4: Univariate analysis of risk factors for major adverse cardiovascular events**

Risk factor	Frequency	P
Age	56.5±14.54	0.042
Male sex	12 (85.7%)	0.278
Diabetes	5 (35.7%)	0.838
Hypertension	6 (42.9%)	0.922
Cerebrovascular accident	2 (14.3%)	0.386
Peripheral vascular disease	2 (14.3%)	0.010
Family history	5 (35.7%)	0.375
Previous myocardial infarction	3 (21.4%)	0.144
Shock	7 (50%)	0.001
Menopause	1 (50%)	0.673
Physical activity	7 (50%)	0.100
Obese	4 (28.6%)	0.625
Waist-hip ratio (>1)	6 (42.9%)	0.185
Current smoker	6 (42.9%)	0.158
Low density lipoprotein (>100 mg/dL)	11 (78.6%)	0.021
Apolipoprotein A1	9 (64.3%)	0.950
Significant CAD	14 (100%)	0.023
Homocysteine	15.47±9	0.868
Hs-CRP	56.67±23	0.002

CAD: coronary artery disease; hs-CRP: high-sensitive C-reactive protein

**Table 5: Multivariate logistic regression for risk factors for major adverse cardiac events**

Independent variable	B	Wald	95% CI		P
			Lower	Upper	
Age	0.024	1.018	0.978	1.073	0.313
Shock	-2.619	8.616	0.013	0.419	0.003
Hs-CRP	0.012	0.844	0.987	1.038	0.358
LDL (>150 mg/dL)	-1.210	2.103	0.058	1.530	0.147

Hs-CRP: high-sensitive C-reactive protein; LDL: low density lipoprotein

shock was found to be a significant determinant of MACE. These findings were in line with previous reports.<sup>19,23,24</sup> The overall in hospital mortality was 9.3%, which was higher than that reported in HP registry (7.6%), CREATE registry (5.6%), and the Kerala registry, which can be explained by our study being limited to a single tertiary center receiving terminal referrals and the limited sample size compared to these studies.<sup>13,16,17</sup>

Acute coronary syndrome is initially diagnosed by primary care physicians. The knowledge of demographic profile, risk factors, and the nature of the disease helps primary physicians in identifying at early stages those who require aggressive management and risk factor modification. With our study, we could identify the demographic profile and risk factor pattern of young and old patients of ACS. Empowered with the findings of this study, primary care physicians could be able to identify those high-risk patients at first contact, and it will help in effective management of ACS patients.

### Study Limitations

The major drawback of this study is the sample size. Moreover, multiple comparisons with small sample size increase the probability of type-1 and type-2 errors. Despite these, the study

has allayed relevant doubts with regards to the demographic and risk factor profile of ACS in young patients. A longer outpatient follow-up after discharge could have added more validity to our observations.

### Conclusion

In conclusion, NSTEMI ACS with atypical angina tends to be more frequent in the young patients with involvement of single-vessel CAD. In elderly patients, Killip class  $\geq 2$  and MACE including in-hospital mortality were higher, and shock was found to be an independent predictor of the MACE during hospital stay.

### Ethics approval and consent to participate

The institutional ethics committee PGIMER Chandigarh has approved the study, with reference number NK/2569/MD/1564-65. Written and informed consent has been taken from the participants.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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