Indian Heart Journal 73 (2021) 295–300

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Epidemiological and clinical profile, management and outcomes of young patients (≤40 years) with acute coronary syndrome: A single tertiary care center study☆

Pruthvi C. Revaiah, Krishna Santosh Vemuri, Rajesh Vijayvergiya, Ajay Bahl, Ankur Gupta, Dinakar Bootla, Ganesh Kasinadhuni, Krishna Prasad Nevali, M. Palanivel Rajan, Lipi Uppal, Atit Gawalkar, Manojkumar Rohit*

Department of Cardiology, Post Graduate Institute of Medical Education & Research, Chandigarh, 160012, India

ARTICLE INFO

Article history:
Received 18 June 2020
Received in revised form
16 November 2020
Accepted 14 January 2021
Available online 17 January 2021

Keywords:
Young adults
Coronary artery disease
Acute coronary syndrome
Epidemiology
Management

ABSTRACT

Objective: To study the epidemiological and clinical profile, angiographic patterns, reasons for the delay in presentation, management, and outcomes of the acute coronary syndrome (ACS) in young patients (≤40yrs) presenting to a tertiary care hospital in North India.

Methods: We included a total of 182 patients aged ≤40 years and presenting with ACS to the cardiology critical care unit of our department from January 2018 to July 2019.

Results: The mean age of the study population was 35.5 ± 4.7years. 96.2% were males. Risk factors prevalent were smoking (56%), hypertension (29.7%), family history of premature coronary artery disease (18.2%), and diabetes (15.9%). The median time to first medical contact and revascularization was 300 (10−43200) minutes and 2880 (75−68400) minutes, respectively. ST-elevation ACS (STE-ACS) accounted for 82% and Non-ST-elevation ACS (NSTE-ACS) accounted for 18% of cases. Thrombolysis was done in 51.7% of the cases. Coronary angiography was done in 91.7% and percutaneous coronary intervention (PCI) in 52.2% (95/182) of the total cases. Coronary artery bypass surgery (CABG) was done in 2 patients (1.1%). Among those who underwent coronary angiography, single-vessel disease (SVD) was seen in 53% of the cases. There were no deaths in hospital, and only one patient died during the 30 days follow up.

Conclusions: STE-ACS was the most common presentation of ACS in the young population. Smoking was the most common risk factor. The majority of the patients had single-vessel disease, and there was a significant delay in first medical contact and revascularization.

1. Introduction

Cardiovascular disease (CVD) is the most common cause of mortality worldwide and in India.[1] Approximately 25% of all the deaths in India are attributable to CVD.[2] Indians are affected by CAD a decade earlier as compared to the western populations.[2–4] In 2016, there were an estimated 62.5 million years of life lost prematurely due to CVD in India.[1]

Due to the epidemiological transition, the prevalence of coronary artery disease (CAD) is rising in young adults.[5] The age cut-off of 40 years was used to define "young" patients with CAD.[6] The clinical and risk factor profile and the coronary artery involvement pattern differs between young CAD patients and those who are elderly.[7,8] Young CAD patients have a good prognosis with a predominance of SVD, and the most common risk factors include smoking, family history of CAD, and hypercholesterolemia.[9] Coronary atherosclerosis is the most common cause (80%) for CAD in the young.[7] Less common reasons for CAD among young adults include coronary vasospasm, medium vessel vasculitis, hypercoagulable states, substance abuse, and embolism, among many other causes.[7] Although CAD in young has a relatively good prognosis, it carries substantial morbidity, psychological impact, financial burden, and more significant loss of Disability-adjusted life years (DALYs) as the

☆ The authors report no financial relationships or conflicts of interest regarding the content herein.

* Corresponding author. Department of Cardiology Level-3, Faculty offices, Advanced Cardiac Center, Post Graduate Institute of Medical Education & Research, Chandigarh, Sector-12, 160012, India.
E-mail address: cardiopgimerchd@gmail.com (M. Rohit).

https://doi.org/10.1016/j.ihj.2021.01.015

young productive age group is being affected.[10] The prevalence of young CAD ranges from 5% to 7% in various registries.[11–13] There have been limited data on the epidemiological and clinical profile and angiographic profile of young adults with ACS in India. Therefore, we sought to evaluate the demographic profile, clinical presentation, echocardiographic and angiographic characteristics, in-hospital outcomes, and 30-day mortality of young adults (≤40 years) with ACS.

2. Materials and methods

2.1. Study design

Our study was a single tertiary care center prospective cross-sectional study of young patients (age ≤40 years) with ACS presenting to the cardiac critical care unit (CCU).

2.2. Material and methods

The study was conducted from January 2018 to June 2019. The study enrolled subjects with acute coronary syndrome and aged ≤40 years. Acute myocardial infarction was defined as per the fourth universal definition of myocardial infarction.[14] NSTE-ACS was defined as per the 2014 American heart association (AHA) NSTE-ACS guidelines.[15] ECG diagnosis of STE-ACS was made in a patient with new ST-segment elevation at the J point in two contiguous leads of ≥0.1 mV in all leads other than leads V2–V3. For leads V2–V3, the criteria taken was ≥0.2 mV in men ≥40 years, ≥0.25 mV in men <40years, or ≥0.15 mV in women.[16] Two dimensional (2D) echocardiography (Vivid Q, GE Healthcare™, New York, USA) was done to assess the left ventricular (LV) systolic function and any mechanical complications. Ejection fraction (EF) was measured using the modified Simpson method. Normal LV function was defined as LVEF of 50–70%, Mild LV dysfunction was defined as LVEF of 40–49%, Moderate LV dysfunction was defined as LVEF of 30–39%, and Severe LV dysfunction was defined as LVEF less than 30%. Cardiogenic shock was defined as systolic blood pressure (SBP) measurements of <90 mm Hg for ≥30 min or the use of drugs or mechanical support to maintain an SBP≥90 mm Hg.[17]

Hypertension was defined based on the 2018 AHA/ACC guidelines for hypertension.[18] Diabetes was described as a fasting blood glucose level of >126 mg/dl or HbA1C of ≥6.5 or a patient already being treated for diabetes mellitus. Smoking was defined as the regular tobacco smoking in any form at present or in the last year. A family history of premature CAD was defined as the documented CAD in a first-degree relative (male <55 years, female <65 years). Modified Kuppuswamy's scale was used for the assessment of socioeconomic status.[19] In-hospital risk assessment was done for ACS groups using thrombolysis in myocardial infarction (TIMI) risk score.[20,21] Dyslipidemia was defined by the presence of any one of the following: LDL >130 mg/dl, Total cholesterol >200 mg/dl and HDL <40 mg/dl in men and <50 mg/dl in women. Obesity was defined as BMI ≥25 kg/m^2. Physical inactivity was defined as non-achievement of physical activity guidelines.[22] Alcohol dependence was determined based on ICD–10 diagnostic guidelines for the dependence syndrome.[23] The MINOCA was defined based on the ESC working group position paper on myocardial infarction with nonobstructive coronary arteries.[24]

Two physicians analyzed the angiographic profiles. >70% stenosis of the left anterior descending artery (LAD), right coronary artery (RCA), or left circumflex artery (LCX), and >50% stenosis of the left main coronary artery (LMCA) was considered obstructive. Patients were monitored until discharge from the hospital to assess outcomes.

2.3. Data collection

Data related to demographics, socioeconomic status, rural/urban background, risk factors, and time to first medical contact/appropriate medical treatment, ACS types, and angiographic profiles, hemodynamics including cardiogenic shock, treatments, and in-hospital and 30 day-mortality rates were recorded.

2.4. Ethical consideration

Institute's ethics committee approved our study protocol, and informed consent was obtained from every patient or appropriate legally authorized relative. The study conforms to the ethical guidelines of the Declaration of Helsinki.

3. Statistical analysis

All the study subjects' data were entered in a Microsoft Excel spreadsheet (Microsoft Excel 2016™, Microsoft Corporation, USA). The data were analyzed using SPSS software (SPSS Inc., version 23.0TM; IBM Corporation, Chicago, USA). Data was collected in a presetproforma. The Kolmogorov–Smirnov test was used to assess continuous variables; the results were median and interquartile range or mean with standard deviations (SD). The significance of differences between the means of normally distributed data was evaluated using the Student's t-test, and that of non-normally distributed data were assessed using the Mann–Whitney U test. Categorical variables were shown as percentages and numbers. Comparison of categorical variables between the study groups was performed by the chi-square test with the Yates' correction for continuity, or the Fisher's exact test if the minimum expected count in the cell was <5. All probability values were calculated using two-sided tests, and a P-value of <0.05 was considered statistically significant.

4. Results

One hundred eighty-two young patients aged ≤40 years with the ACS were included in our study. Table 1 describes the sociodemographic factors and risk factors among the study population. Most of the study population aged between 30 and 40 years. The

Table 1
Sociodemographic factors and risk factors for CAD in young ACS patients.

Variables	n (%)
Mean Age (Years)	35.5 ± 4.7
Total number of patients	182
Sex (%)	
Males	175 (96.2%)
Females	7 (3.8%)
Socioeconomic Status[a]	
Upper	97 (53.3%)
Lower	85 (46.7%)
Area of residence	
Rural	90 (49.5%)
Urban	92 (50.5%)
Risk Factors	
Hypertension	54 (29.7%)
Diabetes Mellitus	29 (15.9%)
Smoking	102 (56%)
Family history of CAD	33 (18.2%)
Physical inactivity	21 (11.5%)
Alcohol dependence	94 (51.8%)

Abbreviations: ACS; Acute coronary syndrome, CAD; Coronary artery disease.
[a] Classification based on modified kuppuswamy scale.

youngest patient aged 18 years. The most common risk factor was smoking. Diabetes and hypertension were not uncommon among the study population. Lipid profile was available in only 56 patients of the study population, out of which 27.2% had dyslipidemia. Tables 2 and 3 describe the clinical profile and coronary angiographic and revascularization patterns of the study population. The most common presenting symptom was angina. STE-ACS was more common as compared to NSTE-ACS. Few patients had the cardiogenic shock and left ventricular failure at presentation. Median TIMI Score among the study population was 2(1–6), while those with cardiogenic shock were 8(3–10) (p<0.001). Among STE-ACS, AWMI was the most common type. All ACS patients were managed with dual antiplatelets, statins, heparin (low molecular weight heparin, unfractionated heparin). Roughly 1/4th had non-obstructive CAD, and 3/4th had obstructive CAD among patients who underwent coronary angiography.

SVD was the most common angiographic pattern, and LAD was the most common vessel involved. Of the 149 patients with STE-ACS, 51.7% underwent thrombolysis. More than half underwent revascularization, and PCI was the most common mode of revascularization. Only 3% of the cohort underwent primary PCI. All patients of ACS were discharged successfully from the hospital. There was no in-hospital mortality. Four patients were readmitted over a three-month follow-up with acute decompensated heart failure (ADHF), and all the four patients had severe left ventricular systolic dysfunction. Of the four patients with ADHF, one patient died due to refractory cardiogenic shock.

Table 4 describes the factors associated with a delayed presentation to the hospital. Of the 182 patients with ACS, only 4.4% presented to the nearest hospital on time (<30mins). None of the patients presented to PCI capable hospitals within 30 min. Only 6.6% came to PCI capable hospitals within 120 min. Patient attitude and surrounding factors were the main factors that contributed to the delayed presentation to the hospital. The median time to first medical contact among study participants was 300(10–43200) minutes. The median time for transport to PCI capable hospital and the median time to a balloon was 1440(60–86400) and 2880(75–68400) minutes.

The median duration of stay in hospital was significantly higher in patients with a cardiogenic shock when compared to patients without cardiogenic shock [4(1–11) v/s 2(1–25) days, p<0.001)]. Patients with cardiogenic shock presented earlier [270(120–7200) v/s 1500(60–86400) minutes, p = 0.009)] to PCI capable hospital and underwent revascularization earlier [1440(240–7200) v/s 3420(75–86400) minutes, p<0.001)] as compared to those without cardiogenic shock as shown in supplementary table 1. Various characteristics of patients with and without cardiogenic shock, STE-ACS, and NSTE-ACS are provided in supplementary tables 1 and 2.

Table 2
Clinical profile of young ACS patients.

Variable	n (%)
Symptoms at presentation	
Angina	180 (98.9%)
Dyspnea	9 (4.9%)
Atypical chest pain	1 (0.5%)
ACS types	
STE-ACS	149 (82%)
1. AWMI	105 (58%)
2. IWMI	41 (23%)
3. LWMI	3 (1%)
NSTE-ACS	33 (18%)
Killip Class	
Class I/II	160 (88%)
Class III/IV	22 (12%)
Complications	
Cardiogenic Shock	13 (7.1%)
Primary ventricular Tachycardia	4 (2.2%)
Complete heart block	2 (1.1%)
Time to FMC (minutes)	300 (10–43200)
Time to revascularization (minutes)	2880 (75–68400)
Thrombolysis	77 (51.7%)
Coronary angiography	167 (91.7%)
PCI	95 (52.2%)
CABG	2 (1.1%)
In-hospital outcomes and follow up	
In-hospital mortality	0
30 day mortality	1 (0.5%)
Complications related to PCI	
Coronary perforation	1(0.5%)
Acute stent thrombosis	1 (0.5%)

Abbreviations: ACS; Acute coronary syndrome, CAD; Coronary artery disease, STE-ACS; ST-elevation ACS, NSTE-ACS; Non-ST-elevation ACS, AWMI; anterior wall myocardial infarction, IWMI; inferior wall myocardial infarction, LWMI; lateral wall myocardial infarction, PCI; Percutaneous coronary intervention, CABG; Coronary artery bypass surgery, FMC; First medical contact.

Table 3
Coronary Angiography profile and Revascularization pattern in the study population.

Variables	n (%)
Obstructive CAD	122 (73%)
Single vessel disease	89 (53%)
1. LAD	68 (40%)
2. LCX	10 (6.3%)
3. RCA	11 (6.7%)
Double vessel disease	20 (12%)
1. LAD and RCA	8 (4.8%)
2. LAD and LCX	9 (5.4%)
3. RCA and LCX	3 (1.8%)
Triple vessel disease	13 (8%)
Left main disease	4 (2.4%)
Non-obstructive CAD	35 (21%)
Normal coronaries	10 (6%)
Spontaneous coronary dissection	7 (3.8%)
1. LAD	5 (2.7%)
2. RCA	2 (1.1%)
MINOCA	17 (10.2%)
Coronary Ectasia	4 (2.4%)
1. LAD	1 (0.6%)
2. All 3 coronaries	3 (1.8%)
Revascularization	99 (54.3%)
1. PCI	95 (52.2%)
2. CABG	2 (1.1%)
3. POBA	2 (1%)
Culprit Vessel PCI	91 (92%)
Non-culprit vessel PCI	17 (12.1%)
Primary PCI	5 (3%)
Rescue PCI	6 (3.6%)

Abbreviations: CAD; Coronary artery disease, LAD; left anterior descending artery LCX; left circumflex artery, RCA; right coronary artery, PCI; Percutaneous coronary intervention, CABG; Coronary artery bypass surgery, POBA; Plain old balloon angioplasty, MINOCA; Myocardial infarction with non-obstructive coronary arteries.

5. Discussion

Our study included 182 patients ≤40 years of age presenting with ACS. CAD in young patients is relatively uncommon. Young patients usually present with the acute coronary syndrome as a manifestation of CAD. The definitions for young CAD in various studies vary.[6] Compared to other communities, south Asians, particularly Indians, are at higher risk of developing CAD at a young age (5–10% v/s 1–2%).[25] The prevalence of CAD is increasing among the young population. However, the details on risk factors and outcomes among young CAD populations, especially ≤40 years of age, is very much limited. Earlier studies have reported a CAD incidence of 3% in ≤40 years of age.[26] In recent data from the

Table 4
Factors associated with the delayed presentation to the hospital (>30 min) (n = 174).

Variable		Individual components	
Patient attitude	86%	1. Do not consider symptoms to be serious	77%
		2. Find it unpleasant/embarrassing to seek medical help	12%
		3. Do not want to be a burden on anyone	12%
Surrounding factors	83%	1. Lack of equipment and proper first-line medications	88%
		2. Living in farther distance from hospital	93%
		3. Lack of suitable transportation	93%
Acute perception of symptoms		**Interpretation of the nature of pain**	
		1. Associate it to the heart problem	12%
		2. Misinterpret the nature of pain	88%
		The reaction during pain occurrence	
		1. Seek medical advice	24%
		2. Pain resistance behavior	76%
Delay phases		1. Symptom onset to decision to seek medical attention	82%
		2. From the decision to seek medical attention to FMC	76%
		3. From FMC to hospital arrival	79%
Reason for a referral to higher center		1. Presentation to PCI capable hospital directly	16%
		2. Lack of CCU/Cath lab	84%

Abbreviations: CCU; Cardiac critical care unit, PCI; Percutaneous coronary intervention, FMC; First medical contact.

YOUNG-MI registry, among patients ≤50 years of age admitted with MI, approximately 20% were ≤40 years.[27] In the GRACE study, the young ACS prevalence was 6.3%,[11] it was 5.8% in the Thai ACS registry,[12] and 7% in the Spanish registry.[13]Among Asians, 4.4% of females and 9.7% of males experience the first instance of MI at <40 years of age.[28]

There are very few registries in India that provide data on the young population's prevalence and profile with CAD. The first registry in India, which published data on the young CAD population, was the CADY registry.[28] In a retrospective study of 8268 patients with ACS from South India, approximately 10% were <40 years of age.[29] Young patients with CAD are almost always males, as reported in many studies.[28–31] Diabetes mellitus and systemic hypertension are well-known risk factors for CAD in the young population, which were evident in our study.[7]

Patients with a history of premature CAD in their families have increased plaque content in their coronaries.[32] The studies from India show a wide variation in the prevalence of a family history of premature CAD, which varies from very low to up to 47%.[29,33,34] Smoking was the most common risk factor for ACS in the young population, similar to other studies.[30,35] Our study found a very high prevalence of alcohol dependence (51.8%) among the study participants, which shows an alarming rise in alcohol consumption among young individuals.[36]

Although many emphasize bringing down the in-hospital delay, the pre-hospital delay was by far the biggest culprit in our study. It may be due to the absence of well-coordinated EMS (emergency medical services) in our country.[37] The various factors responsible for the same are enumerated in Table 4. Our results are similar to multiple ACS registries in India. OASIS 2 registry in 2001 had a pre-hospital delay of 11.8hrs, the CREATE registry in 2008 had a pre-hospital delay of 6hrs, Kerala ACS registry in 2012 had a pre-hospital delay of 4.5hrs respectively.[4,38,39]

While the median time to first medical contact was 6 h, the median time of presentation to PCI capable hospital was 24 h in our study. Most of the patients with ST-elevation myocardial infarction were thrombolysed before presentation to our center and were pain-free. Due to this, there were very few primary PCI.

The most common diagnosis was AWMI (58%) followed by IWMI (23%) and NSTE-ACS (18%), which was similar to prior studies in young ACS patients.[29–31]

Patients with STE-ACS were younger (p<0.001) and had a higher proportion of severe LV systolic dysfunction (p<0.001) as compared to patients with NSTE-ACS. The history of prior CAD was higher in patients with NSTE-ACS as compared to STE-ACS (P = 0.0012).

Angiographic patterns are different in young MI patients as compared to older MI patients. About 1/4th of the population who underwent coronary angiogram had nonobstructive CAD in our study, which was concordant to prior studies.[6,28–31] Seventeen patients (10.2%) were diagnosed as MINOCA, which included seven patients with spontaneous coronary artery dissection, and ten patients with nonobstructive CAD. Twenty-five patients with non-obstructive CAD had STE-ACS and underwent thrombolysis.

Coronary plaque disruption is common among MINOCA patients. The term plaque disruption encompasses plaque rupture and plaque erosion. Plaque disruption can trigger thrombus formation that leads to acute MI via distal embolization, superimposed coronary spasm, and in some cases, complete transient thrombosis with spontaneous thrombolysis.[24] Plaque disruption can only be established with intracoronary imaging, preferably with the higher-resolution optical coherence tomography (OCT) imaging or, to a lesser extent, with intravascular ultrasound (IVUS).[24] Plaque disruption is located in a vessel segment that appears angiographically normal in nearly half of the cases with rupture or ulceration.[24]

Most studies in young ACS patients revealed a predominance of SVD, as seen in the present study.[7,28–31] DVD (12%), TVD (8%), and LM disease (2.4%) were infrequent in the present study re-emphasizing that extensive CAD is rare in a young population with ACS.

No in-hospital deaths were noted, and all patients were discharged in a hemodynamically stable condition. More than 45% were managed medically. These findings show that young adults with ACS have a good prognosis. A comparison of various ACS registries of young patients with age less than or equal to 40 years, including more than 100 patients, is shown in Table 5.[29–31,34,40,41]

6. Limitations

The study is a cross-sectional one without a control group; therefore, each factor's risk and statistical significance could not be analyzed. Risk predictors like lipid profile data were not available in all patients. Intravascular imaging could have accurately demonstrated the underlying cause for CAD (atherosclerotic versus non-atherosclerotic) in these young patients, especially in patients with MINOCA and patients with non-obstructive coronaries.

Table 5
Various studies in India of young (≤40 years) ACS patients.

Study	Age cut-off (Years)	Males (%)	STE-ACS Vs NSTE-ACS (%)	Thrombo–lysis (%)	CAG/PCI (%)	Normal coronaries (%)	Cardiogenic Shock (%)	In-hospital mortality (%)
Bhardwaj et al[30] (n = 124), 2014	40	99%	95% vs 6%	32%	100% vs NA	10.5%	2.41%	1.6%
Prajapati et al[40] (n = 100), 2015	40	96%	85% vs 15%	NA	100% vs NA	22%	NA	NA
Deora et al[29] (n = 820), 2016	40	93%	75% vs 26%	NA	100% vs NA	33%	NA	NA
AMIYA study[34] (n = 1116), 2017	30	95%	100% STE-ACS	55.5%	95% vs 55%	5.2%	4.9%	2.9%
Deshmukh et al[41] (n = 41), 2019	30	95%	100% STE-ACS	61%	100% vs 56%	7.3%	–	2.4%
Gupta et al[31] (n = 102), 2020	35	97%	91% vs 8.8%	32.3%	95% vs 37%	3.1%	1%	2.9%
Present study (n = 182)	40	96%	82% vs 18%	42.3%	92% vs 54%	6%	6.6%	–

Abbreviations: ACS; acute coronary syndrome, CCU; Cardiac critical care unit, PCI; Percutaneous coronary intervention, STE-ACS; ST-elevation ACS, NSTE-ACS; Non-ST elevation ACS, CAG; coronary angiography; NA – Not available.

7. Conclusion

The conventional risk factors are highly prevalent even among young patients with CAD. Despite all the recent advances, delayed presentation in acute coronary syndrome, especially among young patients, is unfortunately widespread. Anterior wall MI is more common, most of the patients have a single-vessel disease, and in-hospital mortality is low in this young population.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ihj.2021.01.015.

References

1. Prabhakaran D, Singh K, Roth GA, Banerjee A, Pagidipati NJ, Huffman MD. Cardiovascular diseases in India compared with the United States. *J Am Coll Cardiol*. 2018;72(1):79–95.
2. Prabhakaran D, Jeemon P, Roy A. Cardiovascular diseases in India: current epidemiology and future directions. *Circulation*. 2016;133(16):1605–1620.
3. Joshi P, Islam S, Pais P, et al. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. *Jama*. 2007;297(3):286–294.
4. Xavier D, Pais P, Devereaux P, et al. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. *Lancet*. 2008;371(9622):1435–1442.
5. Gupta R, Mohan I, Narula J. Trends in coronary heart disease epidemiology in India. *Annals of global health*. 2016;82(2):307–315.
6. Aggarwal A, Srivastava S, Velmurugan M. Newer perspectives of coronary artery disease in young. *World J Cardiol*. 2016;8(12):728.
7. Gulati R, Behfar A, Narula J, et al. Acute myocardial infarction in young individuals. *Mayo Clin Proc*. 2020;95(1):136–156.
8. Badran HM, Elnoamany MF, Khalil TS, Eldin MME. Age-related alteration of risk profile, inflammatory response, and angiographic findings in patients with acute coronary syndrome. *Clin Med Cardiol*. 2009;3:S2118. CMC.
9. Lei L, Bin Z. Risk factor differences in acute myocardial infarction between young and older people: a systematic review and meta-analysis. *International Journal of Cardiovascular Sciences*. 2019;32(2):163–176.
10. Gaziano TA, Bitton A, Anand S, Abrahams-Gessel S, Murphy A. Growing epidemic of coronary heart disease in low-and middle-income countries. *Curr Probl Cardiol*. 2010;35(2):72–115.
11. Avezum A, Makdisse M, Spencer F, et al. Impact of age on management and outcome of acute coronary syndrome: observations from the Global Registry of Acute Coronary Events (GRACE). *Am Heart J*. 2005;149(1):67–73.
12. Tungsubutra W, Tresukosol D, Buddhari W, Boonsom W, Sanguanwang S, Srichaiveth B. Acute coronary syndrome in young adults: the Thai ACS Registry. *J Med Assoc Thai*. 2007;90(Suppl 1):81–90.
13. Morillas P, Bertomeu V, Pabón P, et al. Characteristics and outcome of acute myocardial infarction in young patients. *Cardiology*. 2007;107(4):217–225.
14. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018). *J Am Coll Cardiol*. 2018;72(18):2231–2264.
15. Amsterdam EA, Wenger NK, Brindis RG, et al. AHA/ACC guideline for the management of patients with non–ST-elevation acute coronary syndromes: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64(24):2645–2687, 2014.
16. O'Gara PT, Kushner FG, Ascheim DD, et al. ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American college of cardiology foundation/American heart association task force on practice guidelines. *Circulation*. 2013;127(4). e362–425, 2013.
17. Vahdatpour C, Collins D, Goldberg S. Cardiogenic shock. *Journal of the American Heart Association*. 2019;8(8), e011991.
18. Whelton PK, Carey RM, Aronow WS, et al. ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American college of cardiology/American heart association task force on clinical practice guidelines. Hypertension (dallas, tex : 1979). 2017;71(6):e13–e115, 2018.
19. Bairwa M, Rajput M, Sachdeva S. Modified Kuppuswamy's socioeconomic scale: social researcher should include updated income criteria, 2012. *Indian J Community Med: official publication of Indian Association of Preventive & Social Medicine*. 2013;38(3):185.
20. Morrow DA, Antman EM, Charlesworth A, et al. TIMI risk score for ST-elevation myocardial infarction: a convenient, bedside, clinical score for risk assessment at presentation: an intravenous nPA for treatment of infarcting myocardium early II trial substudy. *Circulation*. 2000;102(17):2031–2037.
21. de Araújo Gonçalves P, Ferreira J, Aguiar C, Seabra-Gomes RTIMI. PURSUIT, and GRACE risk scores: sustained prognostic value and interaction with revascularization in NSTE-ACS. *Eur Heart J*. 2005;26(9):865–872.
22. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public health rep*. 1985;100(2):126–131.
23. Organization WH. *Mental and Behavioural Disorders. Clinical Descriptions and Diagnostic Guidelines. Tenth Revision of the International Classification of Diseases (ICD-10)*. vol. 182. Geneva: WHO; 1992:184.
24. Tamis-Holland JE, Jneid H, Reynolds HR, et al. Contemporary diagnosis and management of patients with myocardial infarction in the absence of obstructive coronary artery disease: a scientific statement from the American Heart Association. *Circulation*. 2019;139(18):e891–e908.
25. Enas EA, Singh V, Munjal Y, Bhandari S, Yadave RD, Manchanda S. Reducing the burden of coronary artery disease in India: challenges and opportunities. *Indian Heart J*. 2008;60(2):161–175.
26. Tsai WC, Wu KY, Lin GM, et al. Clinical characteristics of patients less than forty years old with coronary artery disease in taiwan: a cross-sectional study. *Acta Cardiol Sin*. 2017;33(3):233–240.
27. Yang J, David B, Singh A, et al. Risk factor profiles and outcomes of very young adults with myocardial infarction: results from the YOUNG-MI registry. *J Am Coll Cardiol*. 2019;73(9 Supplement 2):3.
28. Iyengar S, Gupta R, Ravi S, et al. Premature coronary artery disease in India: coronary artery disease in the young (CADY) registry. *Indian Heart J*. 2017;69(2):211–216.
29. Deora S, Kumar T, Ramalingam R, Manjunath CN. Demographic and angiographic profile in premature cases of acute coronary syndrome: analysis of 820 young patients from South India. *Cardiovasc Diagn Ther*. 2016;6(3):193.
30. Bhardwaj R, Kandoria A, Sharma R. Myocardial infarction in young adults-risk factors and pattern of coronary artery involvement. *Niger Med J: journal of the Nigeria Medical Association*. 2014;55(1):44.
31. Gupta MD, Girish M, Kategari A, et al. Epidemiological profile and management patterns of acute myocardial infarction in very young patients from a tertiary care centre. *Indian Heart J*. Jan-Feb 2020;72(1):32–39. https://doi.org/10.1016/j.ihj.2020.03.003. Epub 2020 Mar 2.
32. Otaki Y, Gransar H, Berman DS, et al. Impact of family history of coronary artery disease in young individuals (from the CONFIRM registry). *Am J Cardiol*. 2013;111(8):1081–1086.
33. Pathak V, Ruhela M, Chadha N, Jain S. Risk factors, angiographic characterization and prognosis in young adults presented with acute coronary syndrome at a tertiary care center in North India. *BMR Med*. 2015;1:1–5.
34. Sinha SK, Krishna V, Thakur R, et al. Acute myocardial infarction in very young adults: a clinical presentation, risk factors, hospital outcome index, and their angiographic characteristics in North India-AMIYA Study. *ARYA atherosclerosis*. 2017;13(2):79.
35. Mukherjee D, Hsu A, Moliterno DJ, Lincoff AM, Goormastic M, Topol EJ. Risk factors for premature coronary artery disease and determinants of adverse outcomes after revascularization in patients≤ 40 years old. *Am J Cardiol*. 2003;92(12):1465–1467.

36. Eashwar VA, Umadevi R, Gopalakrishnan S. Alcohol consumption in India—An epidemiological review. *J Fam Med Prim Care*. 2020;9(1):49.
37. Mehmood A, Rowther AA, Kobusingye O, Hyder AA. Assessment of pre-hospital emergency medical services in low-income settings using a health systems approach. *Int J Emerg Med*. 2018;11(1):53.
38. Prabhakaran D, Yusuf S, Mehta S, et al. Two-year outcomes in patients admitted with non-ST elevation acute coronary syndrome: results of the OASIS registry 1 and 2. *Indian Heart J*. 2005;57(3):217–225.
39. Mohanan PP, Mathew R, Harikrishnan S, et al. Presentation, management, and outcomes of 25 748 acute coronary syndrome admissions in Kerala, India: results from the Kerala ACS Registry. *Eur Heart J*. 2013;34(2):121–129.
40. Prajapati J, Joshi H, Sahoo S, Virpariya K, Parmar M, Shah K. Age-related differences of novel atherosclerotic risk factors and angiographic profile among Gujarati acute coronary syndrome patients. *J Clin Diagn Res: J Clin Diagn Res*. 2015;9(6):OC05.
41. Deshmukh PP, Singh MM, Deshpande MA, Rajput AS. Clinical and angiographic profile of very young adults presenting with first acute myocardial infarction: data from a tertiary care center in Central India. *Indian Heart J*. 2019;71(5):418–421.