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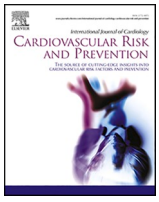

Low body mass index is associated with adverse cardiovascular outcomes following PCI in India: ACC-NCDR registry

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ABSTRACT

Objective: Registry-based prospective study was conducted to evaluate association of body mass index (BMI) with major adverse coronary events (MACE) following percutaneous coronary intervention (PCI).

Methods: Successive patients undergoing PCI were enrolled from April'19 to March'22 and classified into five BMI categories (<23.0,23.0-24.9,25.0-26.9,27.0–29.9, and ≥30.0 kg/m^2). Clinical, angiographic features, interventions and outcomes were obtained by in-person or telephonic follow-up. Primary endpoints were (a) MACE (cardiovascular deaths, acute coronary syndrome or stroke, revascularization, hospitalization and all-cause deaths) and (b)cardiovascular deaths. Cox-proportionate hazard ratios(HR) and 95 % confidence intervals(CI) were calculated.

Results: The cohort included 4045 patients. Mean age was 60.3 ± 11y, 3233(79.7 %) were men. There was high prevalence of cardiometabolic risk factors. 90 % patients had acute coronary syndrome(STEMI 39.6 %, NSTEMI/unstable angina 60.3 %), 60.0 % had impaired ejection fraction(EF) and multivessel CAD. Lower BMI groups (<23.0 kg/m^2) had higher prevalence of tobacco use, reduced ejection fraction(EF), multivessel CAD, stents, and less primary PCI for STEMI. There was no difference in discharge medications and in-hospital deaths. Median follow-up was 24 months (IQR 12–36), available in 3602(89.0 %). In increasing BMI categories, respectively, MACE was in 10.9,8.9,9.5,9.1 and 6.8 % (R^2 = 0.73) and CVD deaths in 5.1,4.5,4.4,5.1 and 3.5 % (R^2 = 0.39). Compared to lowest BMI category, age-sex adjusted HR in successive groups for MACE were 0.89,0.87,0.79,0.69 and CVD deaths 0.98,0.87,0.95,0.75 with overlapping CI. HR attenuated following multivariate adjustments.

Conclusions: Low BMI patients have higher incidence of major adverse cardiovascular events following PCI in India. These patients are older, with greater tobacco use, lower EF, multivessel CAD, delayed STEMI-PCI, and longer hospitalization.

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1. Introduction

Prospective studies have reported that BMI has a U-shaped

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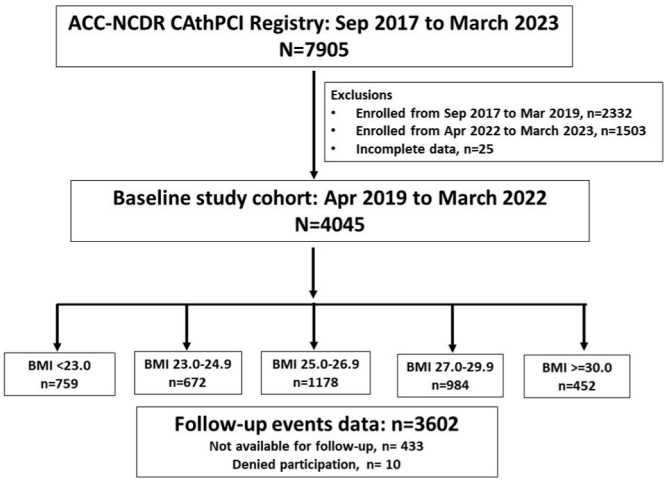

Fig. 1. Flow chart of the patients recruited in ACC-NCDR CAthPCI Registry and participants in the present study.

association with all-cause adverse clinical outcomes and deaths [1–8]. Studies focusing on cardiovascular disease (CVD) have reported linear association of BMI with adverse outcomes (acute coronary syndromes, angina, congestive heart failure, etc) and have mostly been conducted in developed countries of Europe, North and South America and Asia [6,7]. Raised BMI is associated with detrimental effects that include hypertension, diabetes and metabolic syndrome, dyslipidemias (raised triglycerides and low high-density lipoprotein (HDL) cholesterol), sympathetic overdrive, adrenergic stimulation, renin-angiotensin system hyperactivity, etc. [9] Multiple biological changes at the cellular level have also been reported among the overweight and obese [9]. All coronary artery disease (CAD) prevention guidelines highlight importance of weight management and suggest BMI <30.0 kg/m^2 as the primary target [10]. Some Asian and Indian obesity guidelines, along with a WHO consensus statement, recommend BMI target of <25.0 kg/m^2 for obesity and <23.0 kg/m^2 for overweight based on data from regional prospective and cross-sectional studies [11,12].

Level of optimum BMI in secondary prevention of CAD is controversial [13,14]. Observational studies among patients hospitalized with acute coronary syndrome and congestive heart failure have reported that low as well as high BMI are associated with greater mortality and recurrent events at long-term follow-up [15–20]. Some studies have reported that optimum BMI level is 27–30 kg/m^2 and lower and higher levels are associated with adverse outcomes [15–17]. On the other hand, registries from Asia have reported that low BMI is a more important risk factor than high [18–20].

Low BMI, as one of the markers of frailty, has emerged as an important cardiovascular risk factor, both in CAD primary and secondary prevention [21]. Individuals with low BMI, who develop premature CAD have a higher incidence of death due to competing causes [22–24], and in population-based prospective studies, the role of reverse causality cannot be excluded [25]. Previous studies that reported the association of BMI with adverse CAD outcomes following PCI are available from high and upper-middle income countries of Europe, North and South America and Asia [14–20]. No such data are available from India and other lower-middle and low-income developing countries. As part of the American College of Cardiology (ACC) National Cardiovascular Disease Registry (NCDR) program and CathPCI Registry [26], we prospectively record data of all patients who undergo PCI at our hospital [27–29]. To determine risk factors, clinical and angiographic characteristics and treatments, and in-hospital and intermediate-term follow-up outcomes among patients at different levels of BMI we performed this study.

2. Methods

The Cath-PCI Registry at our hospital is part of ACC-NCDR Centre of Excellence program [26]. The registry has been approved by the institutional ethics committee (Government of India, CDSCO Registration No. ECR/615/Inst/RJ/2014/RR-20). Informed consent was obtained from each participant included in the registry with specific consent for inclusion of anonymized data.

Patients: Successive patients undergoing PCI were enrolled over a 36-month period from April 2019 to March 2022 (Fig. 1). This period was used to ensure atleast 12-months follow-up, similar to a previous study [29]. Clinical data were prospectively obtained from admission, at coronary intervention and hospital discharge and entered into the NCDR database. Details of methodology have been previously reported [27–29]. In short, we obtained data regarding age, sex, risk factors-hypertension, diabetes (known or fasting glucose ≥126 mg/dl or random glucose ≥200 mg/dl), hypercholesterolemia (total cholesterol ≥170 mg/dl or non-high-density lipoprotein (HDL) cholesterol ≥100 mg/dl), ever smoking or smokeless tobacco use, chronic kidney disease (admission creatinine ≥2.0 mg/dl), clinical presentation, laboratory investigations, echocardiography for left ventricular ejection fraction (LVEF) and coronary angiography. Data regarding presentation as ST-segment elevation myocardial infarction (STEMI) or non-STEMI (NSTEMI)/unstable angina) were recorded. We also recorded details of the location and extent of CAD on coronary angiography, type of intervention and number of stents deployed. Almost all stents deployed (>99 %) at our hospital are drug-eluting. Details of pre-hospital, in-hospital and post-discharge medications were also recorded. In-hospital follow-up included duration of hospitalization (days) and deaths.

Follow-up: We performed a 12–36 months follow-up of all the patients enrolled from April 2019 to March 2022. In-person follow-up was recommended every 3 months, but due to the ongoing Covid-19 epidemic in India, many patients were not available [29]. Telephonic outcome ascertainment using validated methodology was used in patients not available for in-person follow-up. This methodology is being used in an ongoing prospective study at our centre [30]. Outcomes were locally adjudicated by trained personnel and included in-hospital deaths. The outcomes were classified into (a) major adverse cardiovascular events (MACE): a composite of cardiovascular deaths, myocardial infarction or stroke, coronary revascularization, hospitalization, and all-cause deaths; and (b) cardiovascular deaths. Individual components of primary outcomes were enumerated as secondary outcomes. We also included Covid-19 related deaths as a secondary outcome.

Statistical analyses: All the data are available at ACC-NCDR Cath-PCI registry website [26]. The data have been downloaded from this site and transferred to MS Excel work-sheets. Data analyses have been performed using SPSS software (Version 22.1). Continuous variables are reported as mean ± 1 SD and categorical variables as per cent. Clinical and other characteristics of the whole cohort were first tabulated. The cohort has been categorized into five BMI groups (<23.0, 23.0–24.9, 25.0–26.9, 27.0–29.9, and ≥30.0 kg/m^2). The BMI categories of <25.0 kg/m^2 (ideal weight according to international guidelines) has been classified into two groups (<23.0 and 23.0–24.9 kg/m^2) as advised by WHO Asian consensus [11,12]. Clinical and other details have been tabulated. Inter-group comparisons among BMI categories and trends have been calculated using ANOVA for continuous variables and χ^2 test for categorical variables. We also performed a sensitivity analysis using three BMI groups (<25.0, 25.0–29.9 and ≥ 30.0 kg/m^2) recommended by international guidelines (Supplementary Tables) [9,10]. Follow-up outcomes were determined and Cox regression analysis was performed for calculating proportional hazard ratios (HR) and 95 % confidence intervals (CI). Unadjusted HRs have been calculated with the lowest BMI group (<23.0 kg/m^2) as denominator for comparison with other BMI categories. Subsequently, we calculated HR and 95 % CI following adjustments with (a) age and sex; (b) age, sex and CVD risk factors; and (d)

Table 1
Baseline characteristics of the study cohort recruited from April 2018 to March 2022 in the ACC-NCDR CathPCI Registry.

Variable	Total cohort (n = 4055)
Age (years)	60.3 ± 10.9
Men	3233(79.7)
Women	822(20.3)
Risk factors	
• Hypertension	2237(55.3)
• Diabetes	1649(40.8)
• Cholesterol ≥170 mg/dl	1390(34.4)
• Non-HDL,≥100 mg/dl	2395(59.2)
• Smoking/Tobacco(ever)	381(9.4)
• CKD, creatinine ≥2 mg/dl	91(2.2)
• CAD family history	790(19.5)
• Uninsured status	2235(55.3)
Previous cardiovascular status	
• Coronary intervention (PCI)	568(14.0)
• Coronary bypass surgery	140(3.5)
Acute coronary syndromes	
• STEMI	1603(39.6)
Primary PCI	604(14.9)
Delayed/Rescue PCI	672(16.6)
Pharmaco-Invasive	327(8.1)
• NSTEMI/Unstable angina	2195(54.3)
Chronic coronary syndrome	247(6.1)
Left ventricular ejection fraction (mean)	
• EF <30 %	207(5.1)
• EF 30–45 %	2173(53.7)
• EF >45 %	1665(41.2)
Coronary anatomy and extent	
• Left main coronary artery	235(5.8)
• Right coronary artery	2215(54.8)
• Left anterior descending coronary artery	3280(81.1)
• Left circumflex coronary artery	2139(52.9)
• Single-vessel disease	1521(37.6)
• Double vessel disease	1417(35.0)
• Triple vessel disease	1093(27.0)
Stents deployed	
• Nil	110(2.7)
• 1 stent	2721(67.3)
• 2 stents	959(23.7)
• ≥3 stents	255(6.3)
• Pharmacological vasopressor support	511(12.6)
• Mechanical support (IABP, Impella, ECMO)	152(3.8)
Duration of hospitalization: Median duration (IQR) (hours)	70.1(52.3–90.0)
Discharge medications	
• Dual antiplatelets	3938(97.4)
• Anticoagulant	27(0.7)
• Statins	3962(97.9)
• Beta-blockers	3163(78.2)
• ACEI/ARB	1880(46.5)
In-hospital deaths	61(1.5)

Numbers ± indicate 1 SD. Numbers in parenthesis are percent. CAD coronary artery disease; CKD chronic kidney disease; ECMO extracorporeal membrane oxygenation; HDL high density lipoprotein; IQR interquartile range 25–75; LAD left anterior descending; LCX left circumflex; LDL low density lipoprotein; LMCA left main coronary artery; NSTEMI non ST segment elevation myocardial infarction; RCA right coronary artery; STEMI ST segment elevation myocardial infarction.

multivariate adjustment with age, sex, CVD risk factors, clinical presentation, LVEF, extent of CAD, interventions and duration of hospitalization. P values < 0.05 are considered significant.

3. Results

The ACC-NCDR CathPCI registry at this hospital was initiated in late 2017 and up to March 2023, 7905 patients have been enrolled (Fig. 1). The present study cohort included 4045 patients recruited from April 2019 to March 2022 to facilitate a minimum of 12-month follow-up. The baseline data of this cohort are in Table 1. The mean age of the cohort was 60.3 ± 11 years and a majority of the participants were men (3233, 79.7 %). There was a high prevalence of multiple cardiometabolic risk factors (hypertension, diabetes, hypercholesterolemia, and chronic kidney disease). Previous cardiovascular interventions were PCI in 14.0 % and coronary artery bypass graft (CABG) surgery in 3.5 %. More than 90 % presented with acute coronary syndrome (STEMI 39.6 %, NSTEMI/unstable angina 60.3 %) and 60 % had impaired LVEF (<45 %) at admission. Left anterior descending (LAD) artery was the commonest site of CAD and more than 60 % patients had multivessel disease (double-, triple-, or left main CAD). Multiple coronary stents (≥2) were deployed in 1214 (30.0 %) patients. Pharmacological or mechanical vasopressor support was in 663 (15.4 %) and in-hospital deaths were in 61 (1.5 %) patients.

The cohort has been divided into five BMI categories. Details of clinical characteristics at baseline are in Table 2 and angiographic and in-hospital outcome data are in Table 3. At baseline, the low BMI groups (<23.0 kg/m^2) were older with a mean age of 63.6 ± 11 years compared to other groups ($p < 0.001$). In the low BMI group, there was higher prevalence of smoking/tobacco use and lower prevalence of cardiometabolic risk factors (hypertension, diabetes and hypercholesterolemia). There were insignificant differences in markers of inflammation and previous cardiovascular status in different BMI groups (Table 2). Presentation as NSTEMI/UA was more in higher BMI groups. In low BMI group patients (<23.0 kg/m^2), low LVEF (<30 %) was significantly more as were angiographic left main and triple vessel CAD (Table 3). In low BMI group the rate of primary PCI for STEMI was less and number of stents deployed was lower. The total duration of hospitalization was significantly more in the lowest BMI group patients. There were no differences in discharge medications and in-hospital deaths among the various groups (Table 3).

In-person and telephonic follow-ups were performed for identification and adjudication of various primary and secondary outcome measures. Details of 3602 patients (89.0 %) were available; 433 patients could not be contacted despite repeated attempts and family members of 10 patients refused to provide any information (Fig. 1). A comparison of the baseline data of the total study cohort with those available at the follow-up has been previously reported [29], and showed insignificant differences in various clinical and angiographic features, in-hospital treatment and deaths. Primary outcomes (MACE and cardiovascular deaths) at follow-up are shown in Fig. 2. In increasing BMI categories, respectively, major adverse cardiovascular events were in 10.9, 8.9, 9.5, 9.1 and 6.8 % ($R^2 = 0.73$) and cardiovascular deaths in 5.1, 4.5, 4.4, 5.1 and 3.5 % ($R^2 = 0.39$) (Fig. 2a). Components of the primary outcomes and secondary outcomes are in Table 4 and show no significant inter-group differences. We also classified the patients into three groups based on standard BMI classification criteria (<25.0, 25.0–29.9 and > 30.0 kg/m^2). Baseline characteristics are available as Supplementary Tables 1–3. At follow-up, MACE and CVD deaths in the three groups are shown in Fig. 2b. In escalating BMI groups, respectively, MACE are in 10.0, 9.3 and 6.8 % ($R^2 = 0.90$) and CVD deaths in 4.8, 4.7 and 3.5 % ($R^2 = 0.81$).

To identify the significance of associations of primary outcomes (MACE and CVD deaths) with BMI categories we calculated hazard ratios (HR) and 95 % CI using Cox proportionate hazards model. The lowest BMI group (<23.0 kg/m^2) was used as the reference and univariate, age and sex-adjusted, age, sex and risk factor adjusted, and multivariate adjusted HR and 95 % CI were calculated across the BMI categories. Unadjusted and adjusted HRs are lower in higher BMI categories, with the lowest in BMI group ≥30.0 kg/m^2, compared to low BMI group with significant overlap (Table 4). In the two highest BMI groups the rates of MACE are lower by 21–26 % and 21–33 %, respectively. The HR for CVD deaths are not significant (Fig. 3). The trends completely attenuate following multivariate adjustments for age, sex, CVD risk factors, clinical presentation, LVEF, extent of CAD, interventions and duration of hospitalization (Table 4).

Table 2
Clinical characteristics of patients in different BMI groups.

BMI categories (kg/m^2)	<23.0	23.0–24.9	25.0–26.9	27.0–29.9	≥30.0	X^2trend (p-value)
	N = 759	N = 672	N = 1178	N = 984	N = 452	
Age	63.6 ± 11.6	60.1 ± 10.6	59.5 ± 10.1	59.1 ± 10.8	58.9 ± 11.4	27.0(<0.001)
Men	628(82.7)	549(81.7)	967(82.1)	763(77.5)	316(69.9)	27.3(<0.001)
Risk factors						
Hypertension	400(52.7)	343(51.0)	670(56.9)	535(54.4)	289(63.9)	11.7(0.001)
Diabetes	278(36.6)	258(38.4)	501(42.5)	401(40.8)	211(46.7)	15.1(0.005)
Cholesterol ≥170 mg/dl	215(28.3)	242(36.0)	416(35.3)	365(37.1)	152(33.6)	6.9(0.008)
Non-HDL-C ≥100 mg/dl	419(55.2)	385(57.3)	717(60.9)	606(61.6)	268(59.3)	6.1(0.013)
Smoking/Tobacco ever	95(12.5)	62(9.2)	97(8.2)	77(7.8)	50(11.1)	14.8(0.005)
CKD, creatinine≥2 mg/dl	20(2.6)	14(2.1)	28(2.4)	24(2.4)	05(1.1)	1.2(0.269)
CAD family history	125(16.5)	123(18.3)	220(18.7)	199(20.2)	123(27.2)	16.8(<0.001)
Inflammatory markers						
Current tobacco use	82(10.8)	53(7.8)	88(7.5)	69(7.0)	44(9.7)	4.2(0.039)
Creatinine (mean ± SD)	1.1 ± 0.52	1.0 ± 0.58	1.0 ± 0.56	1.0 ± 0.59	1.0 ± 0.34	1.8(0.114)
White cell (mean ± SD)	9.1 ± 3.4	9.1 ± 3.3	9.5 ± 3.5	9.5 ± 3.5	9.3 ± 3.3	2.5(0.041)
NLR ratio (mean + SD)	4.7 ± 4.4	4.5 ± 4.0	4.8 ± 5.9	4.7 ± 4.9	4.4 ± 5.6	0.89(0.470)
Platelet (mean ± SD)	2.5 ± 0.92	2.5 ± 0.88	2.5 ± 0.91	2.6 ± 0.93	2.7 ± 0.91	2.0(0.084)
HDL-C (mean ± SD)	41.5 ± 10.8	39.6 ± 9.9	39.7 ± 9.6	39.4 ± 9.4	39.3 ± 9.8	6.5(<0.001)
Low HDL <40 mg/dl	349(46.0)	361(53.7)	607(51.5)	536(54.5)	254(56.2)	12.5(<0.001)
Cardiovascular status						
Previous PCI	112(14.8)	95(14.1)	158(13.4)	139(14.1)	04(14.2)	0.12(0.732)
CABG surgery	39(5.1)	22(3.3)	41(3.5)	32(3.3)	06(1.3)	9.6(0.002)
Acute coronary syndrome						
STEMI	305(40.2)	270(40.2)	495(42.0)	380(38.6)	153(33.8)	3.5(0.059)
NSTEMI/UAP	405(53.4)	349(51.9)	608(51.6)	538(56.7)	275(60.8)	7.9(0.005)

Numbers ± indicate 1 SD. Numbers in parenthesis are percent. BMI body mass index; CABG coronary artery bypass graft; CAD coronary artery disease; CHF congestive heart failure; CKD chronic kidney disease; HDL high density lipoprotein; LAD left anterior descending; LCX left circumflex; LDL low density lipoprotein; LMCA left main coronary artery; PCI percutaneous coronary intervention; NLR neutrophil-lymphocyte ratio; NSTEMI non ST segment elevation myocardial infarction; RCA right coronary artery; STEMI ST segment elevation myocardial infarction; UAP unstable angina pectoris.

4. Discussion

This prospective registry shows that in a cohort of CAD patients who underwent percutaneous coronary intervention, lower BMI categories have higher incidence of major adverse cardiovascular events and cardiovascular deaths. Patients in the lower BMI group (<23.0 kg/m2) are older, with greater prevalence of smoking, delayed PCI for STEMI, lower left ventricular function, more multivessel CAD and longer hospitalization.

Studies in the mid and late 20th century from Europe and North America reported that high BMI was a risk factor for cardiovascular events in the general population [2–8], as well as for recurrent events among patients with established CAD [15–17,31–33]. More recent studies from Europe, North America and Asia, on the other hand, have reported that both low and high BMI are associated with an increased risk of recurrent CVD events and deaths in patients with preexisting CAD [18–20,34–38]. This has led to a controversial concept of metabolically healthy obesity [39–41]. Accordingly, a BMI of 27–30 kg/m^2 is considered protective following CAD event [42]. The present study shows that BMI of <23.0 kg/m^2 is associated with more cardiovascular events and deaths following PCI and is different from previous studies in Europe. Studies from Japan, Korea and China have reported that an optimum BMI for these countries could be in the range of 23–27 kg/m^2, while the present study shows that BMI lower than 23.0 kg/m^2 is associated with increased risk while higher BMI is associated with lower risk. We did not have many patients with extreme obesity (BMI ≥35 kg/m^2) and cannot comment on the presence of U-shaped association reported from high-income countries. We also classified our patients into 5 sub-groups which is different from most of the previous studies in Europe and Asia where only 3–4 sub-groups (BMI <25.0, 25.0–29.9, 30.0–34.9 and ≥ 35.0 kg/m^2) were evaluated. This classification is in accordance with Asian consensus statement [11] and Indian guidelines [12], where overweight is defined as BMI 23.0–24.9 kg/m^2, obesity as BMI 25.0–29.9 kg/m^2 and severe obesity as BMI >30.0 kg/m^2. The sample size in the present study is comparable to most studies from Asia and Europe, although the follow-up duration is shorter and event rates lower. There are significant overlaps of confidence intervals in outcomes among various groups and while the differences in MACE are of borderline statistical significance, the differences in CVD deaths are not significant (Table 4). All these are study limitations and larger and more long-term prospective studies from India and other lower-middle-income countries are required to provide more definitive conclusions.

Low BMI and frailty are emerging CAD risk factors [43–47]. Chen et al. reported that there was a U-shaped association between CVD incidence with BMI. Among East Asians, all types of CVD were associated with increased risk at the BMI levels that are lower or higher than 22.5–24.9 kg/m^2 [47]. In South Asian general populations risk of cardiovascular death was more at BMI levels <22.5 and >35.0 kg/m^2 [4]. These results are similar to the findings of the present study where we have reported a greater risk of MACE and CVD deaths at BMI <23.0 with no upper threshold (Fig. 3). A low BMI is associated with multiple pathophysiological features that increase CAD risk. [48]' Lifestyle factors such as smoking and tobacco use, low intake of cardioprotective foods, ambient or household pollution, and presence of chronic inflammation are more in low BMI individuals [48]. Low BMI is also associated with abnormal anthropometric measures (low thigh or hip circumference), sarcopenia and low amount of total fat-free mass. Biological processes associated with low BMI, frailty and aging include cellular senescence and poor status of epigenetic adaptation, telomere maintenance, genomic quality control and repair, proteosis and autophagy, mitochondrial function, inflammation and nutrient and oxygen sensing [49]. We did not assess any of these parameters and other measures of fatness such as abdominal obesity, intra-abdominal fat or subcutaneous fat and this is also a study limitation. Exact characterization of the amount of visceral fat, subcutaneous fat and brown fat requires complex investigations not usually available in a real-world setting as in the present study.

There are several other limitations. This is a single-centre study performed at a tertiary-care dedicated hospital and external validity of the study results, especially in view of low in-hospital and long-term event rates and lower mortality compared to other centres in India

Table 3
Angiographic characteristics, interventions and outcomes among different BMI groups.

BMI categories (kg/m^2)	<23.0	23.0–24.9	25.0–26.9	27.0–29.9	≥30.0	X^2trend (p value)
	N = 759	N = 672	N = 1178	N = 984	N = 452	
LVEF (mean)	44.1 ± 10.6	44.6 ± 10.3	44.7 ± 10.2	45.8 ± 10.2	46.8 ± 9.6	7.1(<0.001)
EF <30 %	52(6.9)	36(5.4)	57(4.8)	43(4.4)	19(4.2)	13.6(<0.001)
EF 30–45 %	412(54.3)	377(56.1)	651(55.3)	512(52.0)	221(48.9)	4.4(0.035)
Coronary angio						
LMCA	55(7.2)	48(7.1)	59(5.0)	50(5.1)	23(5.1)	7.8(0.010)
RCA	404(53.2)	387(57.6)	638(54.2)	535(54.4)	251(55.5)	0.03(0.854)
LAD	623(82.1)	554(82.4)	939(79.7)	802(81.5)	362(80.1)	0.85(0.356)
LCX	430(56.7)	333(49.6)	659(55.9)	503(51.1)	214(47.3)	6.4(0.011)
Single VD	278(36.6)	244(36.3)	443(37.6)	378(38.4)	178(39.4)	1.5(0.223)
Double VD	261(34.4)	242(36.0)	403(34.2)	347(35.3)	164(36.3)	0.19(0.662)
Triple VD	219(28.9)	182(27.1)	329(27.9)	256(26.0)	107(23.7)	3.7(0.056)
STEMI PCI						
Primary PCI	101(13.3)	101(15.0)	186(15.8)	147(14.9)	69(15.2)	0.89(0.345)
Delayed PCI	144(19.0)	115(17.1)	204(17.3)	150(15.2)	59(13.0)	8.0(0.005)
Pharmaco-invasive	60(7.9)	54(8.0)	105(8.9)	83(8.4)	25(5.5)	0.57(0.459)
Stents deployed						
Nil	13(1.7)	22(3.3)	36(3.1)	24(2.4)	15(3.3)	1.2(0.298)
1 stent	511(67.3)	427(63.5)	817(69.4)	670(68.1)	296(65.5)	0.18(0.669)
2 stents	185(24.4)	176(26.2)	268(22.8)	226(23.0)	104(23.0)	1.4(0.238)
≥3 stents	50(6.6)	47(6.9)	57(4.9)	64(6.5)	37(8.2)	0.26(0.608)
Vasopressor use	95(12.5)	98(14.6)	164(13.9)	112(11.4)	42(9.3)	0.18(0.681)
Mechanical support	42(5.5)	18(2.7)	41(3.5)	36(3.6)	15(3.3)	0.29(0.587)
-IABP	40(5.3)	17(2.5)	40(3.5)	35(3.5)	13(2.9)	2.8(0.093)
-Impella	01(0.13)	0(0.0)	01(0.08)	01(0.1)	02(0.44)	1.4(0.111)
-ECMO	01(0.13)	01(0.15)	0(0.0)	0(0.0)	0(0.0)	2.5(0.111)
Hospitalization (hr)						
Mean duration	87.9 ± 73.8	81.5 ± 61.5	83.5 ± 61.4	82.1 ± 67.3	75.5 ± 44.9	2.8(0.023)
Median (IQR)	70.3(52.5–93.4)	70.4(52.3–90.4)	70.4(53.2–90.4)	69.8(52.0–88.9)	66.5(51.1–79.4)	11.5(0.021)
Discharge meds						
Dual antiplatelets	740(97.5)	652(97.0)	1148(97.5	957(97.3)	441(97.6)	0.01(0.938)
Anticoagulant	07(0.9)	05(0.8)	08(0.68)	04(0.41)	03(0.67)	1.1(0.292)
Statins	748(98.5)	656(97.6)	1154(97.9	961(97.7)	443(98.1)	0.02(0.895)
Beta-blockers	586(77.2)	534(79.5)	925(78.5)	772(78.5)	346(76.5)	0.03(0.860)
ACEI/ARB	353(46.5)	309(46.0)	594(50.4)	422(42.9)	202(44.7)	1.5(0.226)
In-hospital deaths	11(1.4)	09(1.3)	23(2.0)	12(1.2)	06(1.3)	0.06(0.803)

Numbers ± indicate 1 SD. Numbers in parenthesis are percent. ACEI angiotensin converting enzyme inhibitors; ARB angiotensin receptor blockers; CAD coronary artery disease; CKD chronic kidney disease; ECMO extra-corporeal membrane oxygenation; EF ejection fraction; HDL high density lipoprotein; IABP intra-aortic balloon pump; IQR interquartile range 25–75; LAD left anterior descending; LCX left circumflex; LDL low density lipoprotein; LMCA left main coronary artery; LVEF left ventricular ejection fraction; PCI percutaneous coronary intervention; NSTEMI non ST segment elevation myocardial infarction; RCA right coronary artery; STEMI ST segment elevation myocardial infarction; VD vessel disease.

[50], can be debated. The proportion of women participants is low but this is similar to data from all over the world, including India [50–52]. The number of patients at extremes of BMI distribution is low and we also did not measure other parameters of body-fat. Abdominal obesity is an important cardiometabolic risk factor in South Asians [12], although the prognostic significance of this feature in patients with established CAD is not clear [47]. A formal frailty assessment was not performed and this could be important in lower BMI individuals with greater CVD events. A prospective study has reported frailty as an important CAD risk factor in South Asians, and frailty was more important in this cohort compared to other regions of the world [25,30,53]. On the other hand this is one of the largest prospective study from India and we used consecutive patients enrolled in ACC-NCDR program which is unique. Low mortality and event rates in the study participants, which is lower than recent registries from India [50], may be indicative of differences in the quality of cardiovascular care.

5. Conclusions

Coronary artery disease is the most important cause of death in India [54]. Our study shows that in a contemporary Indian PCI cohort with low in-hospital and follow-up event rates, a lower BMI (<23.0 kg/m^2) is associated with a higher incidence of major adverse cardiovascular events and deaths. Low BMI patients in this cohort are older, with a higher prevalence of smoking, lower LVEF, left main and triple-vessel CAD, and delayed PCI for STEMI. Frailty could be important, but more research is needed to clarify its role in CAD outcomes [49]. Our study shows that it is not only important to focus on the upper echelons of the BMI spectrum for cardiovascular disease prevention [10], but also consider low BMI as an important risk factor.

CRediT authorship contribution statement

Rajeev Gupta: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Writing - original draft, Writing - review & editing. **Krishna Kumar Sharma:** Data curation, Formal analysis, Project administration, Software, Supervision, Validation, Writing - review & editing. **Raghubir Singh Khedar:** Conceptualization, Writing - review & editing. **Sanjeev Kumar Sharma:** Conceptualization, Data curation, Methodology, Writing - review & editing. **Jitender Singh Makkar:** Conceptualization, Data curation, Methodology, Writing - review & editing. **Ajeet Bana:** Conceptualization, Writing - review & editing. **Vishnu Natani:** Conceptualization, Methodology, Project administration, Resources, Validation. **Shilpa Bharati:** Data curation, Investigation, Methodology. **Sumit Kumar:** Data curation, Investigation, Methodology. **Vishal Hadiya:** Data curation, Investigation, Methodology, Writing - review & editing. **Sailesh Lodha:** Investigation, Methodology, Visualization, Writing - review & editing. **Samin Kumar Sharma:** Conceptualization, Investigation, Methodology, Project administration, Writing - review & editing.

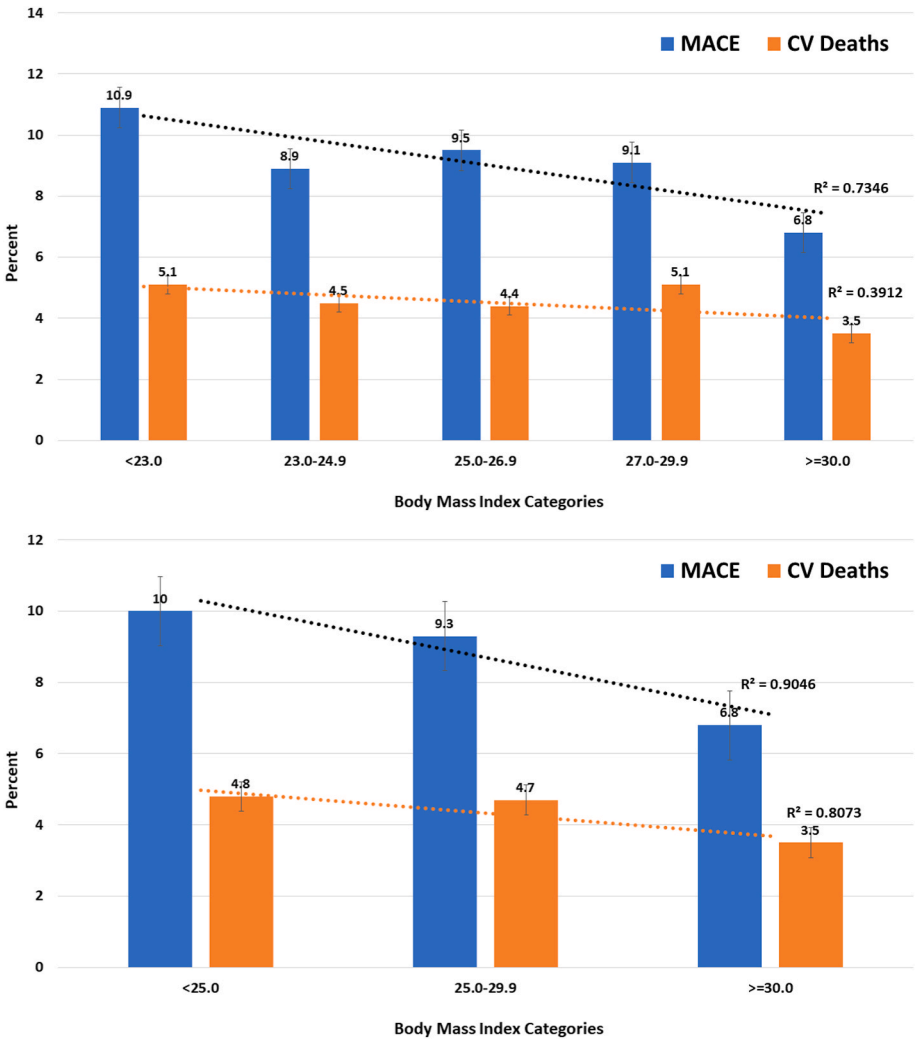

Fig. 2. Major adverse cardiovascular events (MACE) and cardiovascular (CV) deaths at follow-up in different body mass index (BMI, kg/m^2) categories (n = 3602). Classification into five groups (Fig. 2a) shows a weaker association compared to classification into three groups (Fig. 2b).

Table 4
Major adverse cardiovascular events (MACE) and other outcomes in various BMI categories in the follow-up cohort (n = 3602).

BMI categories	Total	<23.0	23.0–24.9	25.0–26.9	27.0–29.9	≥30.0
	N = 3602	N = 691	N = 594	N = 1053	N = 869	N = 395
Primary endpoint (5-point MACE)	334(9.3)	75(10.9)	53(8.9)	100(9.5)	79(9.1)	27(6.8)
Co-Primary endpoint (CVD deaths)	166(4.6)	35(5.1)	27(4.5)	46(4.4)	44(5.1)	14(3.5)
Secondary endpoints						
- All-cause deaths	274(7.6)	60(8.7)	44(7.4)	78(7.4)	70(8.1)	22(5.6)
- Acute coronary syndrome	50(1.4)	10(1.4)	7(1.2)	16(1.5)	9(1.0)	8(2.0)
- Repeat PCI	21(0.58)	9(1.3)	4(0.67)	6(0.57)	2(0.23)	0(0.0)
- CABG surgery	13(0.36)	7(1.0)	1(0.17)	2(0.19)	1(0.11)	2(0.50)
- CVD hospitalizations	198(5.5)	31(4.5)	31(5.2)	60(5.7)	57(6.5)	19(4.8)
- Non-CV hospitalization	106(2.9)	27(3.9)	18(3.0)	35(3.3)	16(1.8)	10(2.5)
- Covid-19 deaths	50(1.4)	6(0.86)	11(1.8)	21(2.0)	9(1.0)	3(0.76)
Univariate hazard ratio (95 % CI)	**MACE**	1.00	0.84(0.59–1.19)	0.80(0.59–1.08)	0.74(0.54–1.02)	0.67(0.43–1.03)
	CVD deaths	1.00	0.91(0.55–1.50)	0.79(0.51–1.23)	0.88(0.56–1.37)	0.72(0.39–1.34)
Age-sex adjusted hazard ratio (95 % CI)	**MACE**	1.00	0.89(0.62–1.26)	0.87(0.64–1.17)	0.79(0.57–1.09)	0.69(0.44–1.07)
	CVD deaths	1.00	0.98(0.59–1.62)	0.87(0.56–1.37)	0.95(0.61–1.50)	0.75(0.40–1.41)
Age-sex, risk factors adjusted hazard ratio (95 % CI)*	**MACE**	1.00	0.90(0.63–1.28)	0.86(0.63–1.17)	0.79(0.57–1.09)	0.69(0.44–1.07)
	CVD deaths	1.00	0.99(0.60–1.65)	0.87(0.56–1.37)	0.96(0.61–1.52)	0.79(0.42–1.48)
Multivariate adjusted hazard ratio (95 % CI)**	**MACE**	1.00	0.93(0.65–1.34)	0.83(0.61–1.13)	0.79(0.57–1.10)	0.79(0.51–1.25)
	CVD deaths	1.00	1.05(0.62–1.76)	0.83(0.53–1.32)	0.96(0.60–1.53)	0.99(0.52–1.89)

MACE (major adverse cardiovascular events (cardiovascular deaths, all-cause deaths, acute coronary syndrome, repeat revascularization and CVD hospitalization); BMI body mass index, CABG coronary artery bypass graft; CI confidence intervals; CVD cardiovascular disease; PCI percutaneous coronary intervention.
*Age, sex and risk factors adjusted hazard ratios; **Multivariate hazard ratios calculated following adjustment for age, sex, risk factors, inflammatory markers, clinical presentation, LVEF, angiographic findings and stents deployed.

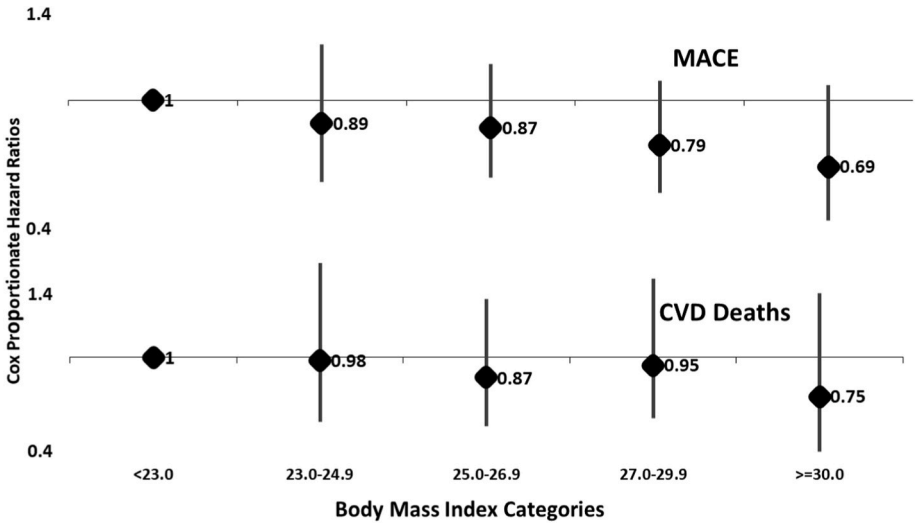

Fig. 3. Age and sex-adjusted Cox proportional hazard ratios and 95 % CI for major adverse cardiovascular events (MACE) and CVD deaths across the BMI categories. The lowest BMI category <23.0 kg/m^2 is the reference.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcrp.2023.200230.

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