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ORIGINAL RESEARCH

In-Hospital Outcomes in Patients With Acute Myocardial Infarction and No Standard Modifiable Cardiovascular Risk Factors Across Varying Body Mass Index: Findings From the CCC-ACS Project

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BACKGROUND: Individuals who present with acute myocardial infarction in the absence of standard modifiable cardiovascular risk factors (ie, SMuRF-less) seem to have a significantly increased risk of mortality; however, it remains unclear whether the "SMuRF paradox" would be influenced by patients' baseline body mass index (BMI) status.

METHODS: Using data from the CCC-ACS (Improving Care for Cardiovascular Disease in China–Acute Coronary Syndrome) project from November 2014 to July 2019, we analyzed patients with acute myocardial infarction with and without SMuRFs and categorized their BMI as underweight (<18.5 kg/m^2), normal weight (18.5–24 kg/m^2), overweight (24–28 kg/m^2), and obese (>28 kg/m^2). The primary outcome was in-hospital all-cause mortality. Multivariable logistic regression models were used to estimate BMI-stratified associations between SMuRF-less status and outcomes.

RESULTS: The study included 44 538 patients with first-presentation acute myocardial infarction, of whom 4454 were SMuRF-less. The incidence of SMuRF-lessness declined from 16.2% to 6.5% as BMI increased by category, and it prevailed more frequently among women and older people regardless of their BMI status. Patients who were SMuRF-less had a significant increase in in-hospital mortality than patients with ≥1 SMuRF (adjusted odds ratio [OR], 1.750 [95% CI, 1.057–2.896], P<0.001). The highest mortality rate was observed in the group who were SMuRF-less and underweight (3.5%). Considering patients with ≥1 SMuRF and obesity as the reference group, the group who were SMuRF-less underweight exhibited the highest increase in mortality (adjusted OR, 3.854 [95% CI, 2.130–6.973], P<0.001).

CONCLUSIONS: Among patients with first-presentation acute myocardial infarction, compared with those with ≥1 SMuRF, patients who were SMuRF-less have a significantly higher risk of in-hospital mortality, especially in those underweight, whereas in-hospital survival was the most favorable among patients with ≥1 SMuRF and obesity.

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Key Words: acute myocardial infarction ■ body mass index ■ in-hospital mortality ■ standard modifiable cardiovascular risk factors

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CLINICAL PERSPECTIVE

What Is New?

- This study of large-scale multicenter data from a comprehensive national registry is the first to examine the body mass index-stratified disparities in the standard modifiable cardiovascular risk factors (SMuRFs) paradox among patients with first-presentation acute myocardial infarction.
- In-hospital survival following acute myocardial infarction was least favorable among individuals in the absence of standard modifiable cardiovascular risk factors and combined with underweight, whereas the outcome was the most favorable among those with at least 1 standard modifiable cardiovascular risk factor and obesity.

What Are the Clinical Implications?

- This study emphasized the importance of identifying patients' standard modifiable cardiovascular risk factors profile and body mass index status at admission when stratifying risk management as we move toward more individualized acute myocardial infarction care.

Nonstandard Abbreviations and Acronyms

CCC-ACS	Improving Care for Cardiovascular Disease in China–Acute Coronary Syndrome
SMuRF-less	no standard modifiable cardiovascular risk factors
SMuRFs	standard modifiable cardiovascular risk factors

The pioneering Framingham Heart Study and various subsequent epidemiologic studies have contributed transformative discoveries on predisposing factors of coronary heart disease over the past 7 decades[1,2]; diabetes, hypercholesterolemia, hypertension, and smoking, which are well recognized as the standard modifiable cardiovascular risk factors (SMuRFs), have led to major improvements in the coronary heart disease prevention system.[3–5] However, recent studies revealed a counterintuitive fact that patients with acute myocardial infarction (AMI) in the absence of SMuRFs (ie, SMuRF-less) exhibit a higher mortality rate than those with at least 1 of the SMuRFs.[5–12] These findings contradict a general sense of complacency that the adverse outcome of AMI can be predominantly avoided when people can adequately manage their modifiable risk factors. Studies focusing on interpreting the SMuRF paradox observed in AMI patients have been crucial for squarely acknowledging the value of coronary heart disease risk factors and shaping public health policies targeting these.

Body mass index (BMI) has long been adopted as an essential sign in clinical practice to assess body health and conduct metabolic risk stratification[13,14]; it generally displays a U-shaped pattern correlated with morbidity or mortality, indicating that extreme BMI tends to be associated with worse outcomes.[15–17] SMuRF-less and abnormal BMI coexisting are not rare among patients with AMI, but their combined prognostic implications on cardiovascular outcomes remain poorly explored. Here, we examined the SMuRF paradox across the BMI spectrum using the CCC-ACS (Improving Care for Cardiovascular Disease in China–Acute Coronary Syndrome) project, which is the largest ongoing nationwide quality improvement registry for ACS in China, aiming to unveil BMI-related disparities in the SMuRF paradox among patients with first-presentation AMI. These findings may help better conduct risk factor screening and prevention as we move toward more individualized AMI care.

METHODS

Study Design and Population

The data that support the findings of this study are available from Beijing Anzhen Hospital but restrictions apply to the availability of these data, which were used under license for the current study and so are not publicly available. As a collaborative initiative of the American Heart Association and the Chinese Society of Cardiology, the CCC-ACS project is a national hospital-based registry program for patients with ACS. The project was launched in 2014 and included 159 tertiary hospitals and 82 secondary hospitals from different geographic and economic regions of China, focusing on improving the quality of care. Details on the design and methodology of the CCC-ACS project have been published elsewhere.[18] The study was conducted in accordance with the Declaration of Helsinki. The CCC-ACS project was approved by the institutional review board of Beijing Anzhen Hospital and the need for informed consent was waived as the retrospective nature of the study. From November 2014 to July 2019, a total of 104 516 patients with ACS were enrolled.

Patients included in the current study were 18 years or older with the first occurrence of AMI. Patients with a known history of percutaneous coronary intervention, coronary artery bypass graft, or MI were excluded; missing records for SMuRFs or BMI were also excluded. The ethics committee of Beijing Anzhen

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Hospital, Capital Medical University, China, granted institutional review board approval for this research with a waiver for informed consent. Of the 94 623 participants with AMI who were registered in the CCC-ACS project from 2014 to 2019, 50 085 were excluded for 1 or more of the following reasons at baseline: a known history of percutaneous coronary intervention (n=9657), a known history of coronary artery bypass graft (n=593), or a known history of myocardial infarction (n=9528); a further 30 307 patients were excluded because of missing data on SMuRF or BMI at baseline. The ultimate sample consisted of 44 538 participants with first-presentation AMI.

Definitions

Definitions of SMuRFs were based on electronic medical records, hospital findings, and patient self-report on smoking during admission. Diabetes was defined as having a prior diagnosis of diabetes or previous hypoglycemic therapy. Hypertension was defined as having a prior diagnosis of hypertension, previous antihypertensive pharmacotherapy, or a new diagnosis of hypertension during the index admission. As both fasting glucose and acute-phase blood pressure are influenced by neurohormonal response to AMI, these were not incorporated in the definitions. Hypercholesterolemia was defined by known low-density lipoprotein cholesterol >135 mg/dL (3.5 mmol/L) or total cholesterol >213 mg/dL (5.5 mmol/L) or having an ongoing cholesterol-lowering treatment at admission. Current smokers were identified if they had smoked within the past year before the index hospitalization. Height and weight were retrieved from electronic medical records. BMI was calculated as weight in kilograms divided by height in square meters. Patients were stratified into the BMI classification adherence to the current criteria in China[19]: underweight (<18.5 kg/m^2), normal weight (18.5 to <24 kg/m^2), overweight (24 to <28 kg/m^2), and obesity (≥28 kg/m^2).

Outcomes

The primary outcome was in-hospital mortality. Secondary outcomes were in-hospital major adverse cardiovascular events (MACEs), defined as a composite end point of all-cause death, cardiac shock, acute congestive heart failure, reinfarction, or stroke during hospitalization.

Statistical Analysis

Categorical variables were summarized as frequencies and percentages; numerical variables were summarized as the mean±SD or median (interquartile range), depending on the data distribution. Categorical variables were compared with the χ^2 test, and continuous variables with Mann–Whitney nonparametric tests. The associations between the variables and the binary study outcomes were assessed using multivariable logistic regression models with an odds ratio (OR) and 95% CI in the total population and by stratified groups. Potential covariates were identified by reviewing existing literature and clinician consensus; the following variables were extracted from the baseline assessment data: demographic factors (age and sex); clinical characteristics (heart rate, diagnosed ST-segment–elevation MI [STEMI], low-density lipoprotein cholesterol, serum creatinine, left main coronary artery disease, and multivessel coronary artery disease); prehospital pharmacotherapy (antiplatelets and statins); and in-hospital management (intracoronary therapy, dual-antiplatelet therapy, and statins); their correlation with in-hospital mortality and total MACEs was displayed in Table S1. The assumption of regression analysis was checked by examining the interaction term between the SMuRF-BMI status. A 2-sided *P* value of <0.05 was considered to indicate statistical significance. All statistical analyses were performed with SPSS version 24 (SPSS Statistics, IBM Corp, Armonk, NY, USA).

RESULTS

Table 1 displays the baseline characteristics and absolute event numbers for all participants. In total, 35 249 (79%) of 44 538 participants were male, the median age was 61 years (range 52–68 years), and the median BMI was 24 kg/m^2 (range 22–26 kg/m^2). In patients with at least 1 SMuRF (n=40 084), the most common SMuRF was current smoking (53.4%), followed by hypertension (52.6%), hypercholesterolemia (46.0%), and diabetes (25.7%). Patients who were SMuRF-less were less likely to have a history of cerebrovascular disease, family history of coronary heart disease, or prescription of guideline-directed medical therapy; they had significantly lower hemoglobin, low-density lipoprotein cholesterol, total cholesterol, and triglycerides than patients with SMuRFs; there was no difference in the rate of thrombolysis, thrombus aspiration, or coronary artery bypass graft between the 2 groups. As shown in Figure 1, SMuRF-lessness was observed in 4454 (10.0%) of the total participants, with the incidence of 16.2%, 11.6%, 9.0%, and 6.5% in BMI categories of <18.5 kg/m^2, 18.5 to 24 kg/m^2, 24 to 28 kg/m^2, and ≥28 kg/m^2, respectively; compared with the group with ≥1 SMuRF, SMuRF-less status was significantly more common in women than men and older people than younger people, regardless of the BMI groups (all *P*<0.02, seen in Table S2). During the median hospital stay of 9 days (7–12 days), 3501 (7.9%) total MACEs (8.9% in the SMuRF-less category and 7.7% in the ≥1 SMuRF category, *P*=0.007) and 491 (1.1%) all-cause

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Table 1. Baseline Characteristics, In-Hospital Management, and Outcomes of Patients With Different SMuRF-BMI Status

Variable	Total population (n=44 538)	SMuRF-less (n=4454)					≥1 SMuRFs (n=40 084)					*P* value*
		All BMI categories (n=4454)	BMI<18.5 (n=173)	18.5≦BMI<24 (n=2178)	24≦BMI<28 (n=1765)	BMI≧28 (n=338)	All BMI categories (n=40 084)	BMI<18.5 (n=897)	18.5≦BMI<24 (n=16 546)	24≦BMI<28 (n=17 813)	BMI≧28 (n=4828)	
Admission characteristics												
Age, y	61 (52–68)	62 (53–69)	67 (61–73)	64 (55–70)	61 (51–68)	56 (48–65)	60 (52–67)	67 (61–72)	62 (54–69)	60 (51–67)	55 (47–64)	<0.001
Sex, male, n (%)	35 249 (79.1)	3210 (72.0)	98 (57.0)	1520 (70.0)	1335 (75.6)	257 (76.0)	32 039 (80.0)	592 (66.0)	12 865 (77.8)	14 647 (82.2)	3935 (82.0)	<0.001
Heart rate, bpm	76 (67–86)	76 (66–86)	78 (68–90)	75 (66–85)	76 (67–85)	78 (68–88)	76 (68–86)	76 (66–86)	76 (67–86)	76 (68–86)	78 (68–89)	0.004
Systolic blood pressure, mm Hg	129 (114–144)	120 (109–135)	120 (106–131)	120 (108–134)	121 (110–136)	121 (110–137)	130 (115–145)	127 (110–145)	128 (112–144)	130 (115–145)	133 (119–150)	<0.001
Diastolic blood pressure, mm Hg	79 (70–89)	75 (67–83)	73 (63–82)	74 (66–82)	76 (69–84)	78 (69–87)	79 (70–90)	76 (67–87)	78 (69–88)	80 (70–90)	80 (71–92)	<0.001
Body mass index, kg/m^2	24.2 (22.5–26.2)	23.8 (21.9–25.6)	17.7 (16.9–18.2)	22.1 (20.8–23.1)	25.4 (24.5–26.3)	29.4 (28.4–30.9)	24.3 (22.5–26.3)	17.7 (17.0–18.1)	22.4 (21.2–23.2)	25.5 (24.7–26.5)	29.4 (28.7–31.1)	<0.001
SMuRFs status, n (%)												
Hypertension	21 100 (47.4)						21 100 (52.6)	416 (46.4)	8013 (48.4)	9671 (54.3)	3000 (62.1)	
Diabetes	10 281 (23.1)						10 281 (25.7)	173 (19.3)	3865 (23.4)	4763 (26.7)	1480 (30.1)	
Hypercholesterolemia	18 436 (41.4)						18 436 (46.0)	384 (42.8)	7491 (45.3)	8142 (45.7)	2419 (50.1)	
Current smoking	21 417 (48.1)						21 417 (53.4)	422 (47.0)	8704 (52.6)	9638 (54.1)	2653 (55.0)	
Cerebrovascular disease, n (%)	3230 (7.3)	153 (3.4)	10 (5.8)	84 (3.9)	51 (2.9)	8 (2.4)	3077 (7.7)	71 (7.9)	1243 (7.5)	1387 (7.8)	376 (7.8)	<0.001
Family history of CAD, n (%)	1413 (3.2)	61 (1.4)	3 (1.7)	19 (0.9)	32 (1.8)	7 (2.1)	1352 (3.4)	24 (2.7)	415 (2.5)	672 (3.8)	241 (5.0)	<0.001
Chronic obstructive pulmonary disease, n (%)	446 (1.0)	45 (1.0)	5 (2.8)	23 (1.0)	14 (0.7)	3 (0.8)	401 (1.0)	30 (3.3)	190 (1.1)	145 (0.8)	36 (0.7)	0.945
Prehospital pharmacotherapy												
Antiplatelets, n (%)	8318 (18.7)	418 (9.4)	14 (8.1)	191 (8.8)	169 (9.6)	44 (13.0)	7900 (19.7)	227 (25.3)	3325 (20.1)	3405 (19.1)	943 (19.5)	<0.001
Aspirin, n (%)	7495 (16.8)	359 (8.1)	13 (7.5)	163 (7.5)	155 (8.8)	28 (8.3)	7136 (17.8)	209 (23.3)	2997 (18.1)	3080 (17.3)	850 (17.6)	<0.001
$P2Y_{12}$ inhibitor, n (%)	6092 (13.7)	297 (6.7)	8 (4.6)	142 (6.5)	112 (6.3)	35 (10.4)	5795 (14.5)	182 (20.3)	2488 (15.0)	2444 (13.7)	681 (14.1)	<0.001
Statin, n (%)	5690 (12.8)						5690 (14.2)	167 (18.6)	2435 (14.7)	2405 (13.5)	683 (14.1)	
β-blocker, n (%)	3350 (7.5)	45 (1.0)	2 (1.2)	21 (1.0)	19 (1.1)	3 (0.9)	3305 (8.2)	40 (4.5)	1202 (7.3)	1547 (8.7)	516 (10.7)	<0.001
ACEI/ARB, n (%)	3589 (8.1)	50 (1.1)	2 (1.2)	22 (1.0)	23 (1.3)	3 (0.9)	3539 (8.8)	63 (7.0)	1274 (7.7)	1662 (9.3)	540 (11.2)	<0.001
Acute myocardial infarction presentation												
ST-segment–elevation myocardial infarction, n (%)	31 603 (71.0)	3294 (74.0)	125 (72.3)	1616 (74.2)	1317 (74.6)	236 (69.8)	28 309 (70.6)	630 (70.2)	11 866 (71.7)	12 545 (70.4)	3268 (67.7)	<0.001
Killip class>I, n (%)	2784 (6.3)	264 (5.9)	19 (11.0)	135 (6.2)	89 (5.0)	21 (6.2)	2484 (12.4)	70 (7.8)	1120 (6.8)	1016 (5.7)	278 (5.8)	0.478
II–III	2307 (5.2)	205 (4.6)	17 (9.8)	102 (4.7)	70 (4.0)	16 (4.7)	2102 (5.2)	55 (6.1)	943 (5.7)	856 (4.8)	248 (5.1)	0.067
IV	441 (1.0)	59 (1.3)	2 (1.2)	33 (1.5)	19 (1.1)	5 (1.5)	382 (1.0)	15 (1.7)	177 (1.1)	160 (0.9)	30 (0.6)	0.017

(*Continued*)

Table 1. Continued

Variable	Total population (n=44538)	SMuRF-less (n=4454)					≥1 SMuRFs (n=40084)					*P* value*
		All BMI categories (n=4454)	BMI<18.5 (n=173)	18.5≦BMI<24 (n=2178)	24≦BMI<28 (n=1765)	BMI≧28 (n=338)	All BMI categories (n=40084)	BMI<18.5 (n=897)	18.5≦BMI<24 (n=16546)	24≦BMI<28 (n=17813)	BMI≧28 (n=4828)	
Laboratory, echocardiographic and angiographic data												
Hemoglobin, g/L	140 (127–152)	136 (123–148)	128 (115–139)	134 (121–145)	139 (126–151)	144 (128–153)	140 (128–152)	130 (116–143)	138 (126–150)	142 (130–154)	145 (133–157)	<0.001
Triglycerides, mg/dL	58.8 (41.0–87.4)	50.0 (34.8–71.2)	37.1 (24.7–57.6)	46.8 (33.6–66.1)	52.6 (37.1–75.4)	56.8 (41.4–82.0)	59.9 (42.2–89.3)	45.4 (32.5–65.0)	1.43 (1.01–2.13)	55.3 (39.1–82.4)	70.0 (49.5–104.8)	<0.001
Total cholesterol, mg/dL	172.1 (143.6–201.9)	160.1 (136.1–179.4)	156.2 (133.8–175.6)	160.1 (135.7–178.3)	159.7 (136.5–181.4)	162.4 (138.4–182.1)	174.01 (45.0–205.3)	168.6 (135.3–200.7)	172.9 (144.2–205.0)	172.9 (144.2–205.0)	177.5 (149.7–208.4)	<0.001
Low-density lipoprotein cholesterol, mg/dL	105.6 (83.1–130.3)	94.7 (77.3–111.4)	88.2 (73.5–101.7)	94.0 (75.8–111.0)	95.1 (78.1–112.1)	99.0 (82.4–116.4)	107.1 (83.9–113.0)	97.4 (75.4–125.7)	106.0 (82.8–132.6)	106.0 (82.8–132.6)	109.8 (87.0–134.6)	<0.001
High-density lipoprotein cholesterol -C, mg/dL	39.8 (33.3–48.0)	41.0 (34.4–49.1)	46.0 (37.5–56.1)	42.2 (35.6–50.7)	39.8 (33.3–47.6)	37.5 (32.5–46.0)	39.4 (33.3–47.6)	44.5 (36.0–54.5)	41.0 (34.0–49.1)	41.0 (34.0–49.1)	37.1 (31.7–44.9)	<0.001
Creatinine, μmol/L	80 (67–96)	76 (63–92)	72 (58–87)	75 (63–91)	77 (64–93)	78 (66–93)	80 (67–97)	78 (63–98)	79 (66–97)	80 (68–96)	81 (68–97)	<0.001
Glycated hemoglobin A1c, %†	6.0 (5.8–7.0)	5.8 (5.7–6.1)	6.0 (5.4–6.1)	6.0 (5.7–6.1)	6.0 (5.8–6.1)	5.8 (5.5–6.2)	6.1 (5.6–7.4)	5.9 (5.5–6.6)	5.9 (5.5–6.6)	5.9 (5.5–6.6)	6.3 (5.7–7.7)	<0.001
Troponin T, ng/mL‡												
Baseline value	0.7 (0.1–3.7)	0.8 (0.2–3.6)	0.7 (0.1–4.3)	0.9 (0.2–3.7)	0.8 (0.2–3.7)	0.5 (0.1–2.5)	0.7 (0.1–3.8)	0.8 (0.2–3.7)	0.8 (0.1–4.3)	0.7 (0.1–3.8)	0.5 (0.1–2.5)	0.328
Peak value	2.0 (0.5–6.8)	2.1 (0.6–6.2)	2.5 (0.7–10.0)	2.0 (0.5–6.1)	2.3 (0.6–6.4)	1.8 (0.5–4.5)	2.0 (0.5–6.9)	1.7 (0.4–6.8)	2.1 (0.5–7.5)	2.1 (0.5–6.8)	1.7 (0.5–5.7)	0.738
Troponin I, ng/mL§												
Baseline value	2.0 (0.2–13.3)	2.1 (0.2–13.8)	2.4 (0.2–12.7)	2.3 (0.3–14.4)	2.2 (0.2–12.9)	1.5 (0.1–8.7)	2.0 (0.2–13.2)	2.4 (0.4–14.3)	2.4 (0.3–15.0)	1.8 (0.2–12.7)	1.5 (0.2–10.1)	0.662
Peak value	8.7 (1.3–32.1)	8.4 (1.2–30.0)	10.6 (1.2–33.8)	8.8 (1.2–28.7)	7.9 (1.4–30.0)	7.3 (1.0–28.0)	8.8 (1.3–32.4)	7.4 (1.0–26.0)	9.2 (1.4–33.0)	8.7 (1.3–12.7)	8.0 (1.2–31.2)	0.124
Left ventricular systolic dysfunction (EF <50%), n (%)‖	8562 (19.2)	813 (18.3)	33 (19.1)	431 (19.8)	294 (16.7)	55 (16.3)	7749 (19.3)	205 (22.9)	3385 (20.5)	3346 (18, 8)	813 (16.8)	0.083
Left main coronary artery disease, n (%)	1521 (3.4)	172 (3.9)	5 (2.9)	85 (3.9)	71 (4.0)	11 (3.3)	1349 (3.4)	20 (2.2)	589 (3.6)	604 (3.4)	136 (2.8)	0.084
Multivessel coronary artery disease, n (%)	10929 (24.5)	980 (22.0)	30 (17.3)	481 (22.1)	395 (22.4)	74 (21.9)	9949 (24.8)	202 (22.5)	3884 (23.5)	4589 (25.8)	1274 (26.4)	<0.001
In-hospital management												
Thrombolysis, n (%)	1648 (3.7)	188 (4.2)	8 (4.6)	94 (4.3)	78 (4.4)	8 (2.4)	1460 (3.6)	39 (4.3)	620 (3.7)	664 (3.7)	137 (2.8)	0.052
Intracoronary procedures, n (%)	31671 (71.1)	3029 (68.0)	104 (60.1)	1450 (66.6)	1240 (70.3)	235 (69.5)	28642 (71.5)	562 (62.7)	11784 (71.2)	12804 (71.9)	3492 (72.3)	<0.001
Thrombus aspiration, n (%)	4625 (10.4)	473 (10.6)	12 (6.9)	216 (9.9)	202 (11.4)	43 (12.7)	4152 (10.4)	58 (6.5)	1610 (9.7)	1996 (11.2)	488 (10.1)	0.587
PCI, n (%)	35971 (80.8)	3467 (77.8)	115 (66.5)	1648 (75.7)	1432 (81.1)	272 (80.5)	32504 (81.1)	618 (68.9)	13277 (80.2)	14662 (82.3)	3947 (81.8)	<0.001
PCI route, n (%)#												
Radial	24190 (67.2)	2419 (70.0)	76 (43.9)	1141 (52.4)	1020 (71.2)	182 (66.9)	21771 (54.3)	414 (46.2)	9043 (54.7)	9779 (54.9)	2535 (52.5)	0.505
Femoral	1279 (3.6)	115 (3.3)	1 (0.6)	57 (3.5)	45 (3.1)	5 (1.5)	1164 (2.9)	33 (3.7)	471 (2.8)	525 (2.9)	135 (2.8)	0.238

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Table 1. Continued

Variable	Total population (n=44538)	SMuRF-less (n=4454)					≥1 SMuRFs (n=40084)					*P* value*
		All BMI categories (n=4454)	BMI<18.5 (n=173)	18.5≦BMI<24 (n=2178)	24≦BMI<28 (n=1765)	BMI≧28 (n=338)	All BMI categories (n=40084)	BMI<18.5 (n=897)	18.5≦BMI<24 (n=16546)	24≦BMI<28 (n=17813)	BMI≧28 (n=4828)	
Coronary artery bypass grafting, n (%)	321 (0.7)	27 (0.6)	1 (0.6)	19 (0.9)	7 (0.4)	0 (0)	294 (0.7)	10 (1.1)	126 (0.8)	128 (0.7)	30 (0.6)	0.341
Medical therapy, n (%)												
Dual antiplatelet therapy	42305 (95.0)	4145 (93.1)	154 (89.0)	2029 (93.2)	1645 (93.2)	317 (93.8)	38160 (95.2)	823 (91.8)	15668 (94.7)	17048 (95.7)	4621 (95.7)	<0.001
Aspirin	42907 (96.3)	4206 (94.4)	159 (91.9)	2057 (94.4)	1670 (94.6)	320 (94.7)	38701 (96.5)	837 (93.3)	15865 (95.9)	17229 (96.7)	4670 (96.7)	<0.001
$P2Y_{12}$ inhibitor	42917 (96.4)	4219 (94.7)	159 (91.9)	2072 (95.1)	1666 (94.4)	322 (95.3)	38698 (96.5)	852 (95.0)	15940 (96.3)	17226 (96.7)	4680 (96.9)	<0.001
Glycoprotein IIb/IIIa	14121 (31.7)	1320 (29.6)	58 (33.5)	618 (28.4)	545 (30.9)	99 (29.3)	12801 (31.9)	210 (23.4)	5009 (30.3)	5888 (33.1)	1694 (35.1)	0.002
Heparin	33944 (76.4)	3269 (73.4)	115 (66.5)	1569 (72.0)	1342 (76.0)	243 (71.9)	30675 (76.8)	660 (73.6)	12369 (74.8)	13850 (78.3)	3796 (78.6)	<0.001
Statin	42166 (94.7)	4093 (91.9)	155 (89.6)	2003 (92.0)	1632 (92.5)	303 (89.6)	38073 (95.0)	843 (94.0)	15680 (94.8)	16935 (95.1)	4615 (95.6)	<0.001
β-blocker	25232 (56.7)	2263 (50.8)	76 (43.9)	1070 (49.1)	915 (51.8)	202 (59.8)	22969 (57.3)	472 (52.6)	9088 (54.9)	10378 (58.3)	3031 (62.8)	<0.001
ACEI/ARB	21614 (48.5)	1638 (36.8)	56 (32.4)	787 (36.1)	659 (37.3)	136 (40.2)	19976 (49.8)	381 (42.5)	7762 (46.9)	9052 (50.8)	2781 (57.6)	<0.001
In-hospital outcomes												
MACEs, n (%)**	3501 (7.9)	396 (8.9)	22 (12.7)	214 (9.8)	135 (7.6)	25 (7.4)	3105 (7.7)	105 (11.7)	1390 (8.4)	1298 (7.3)	312 (6.5)	0.007
All-cause death	491 (1.1)	95 (2.1)	6 (3.5)	52 (2.4)	30 (1.7)	7 (2.1)	396 (1.0)	13 (1.4)	171 (1.0)	187 (1.0)	25 (0.5)	<0.001
Cardiac shock or acute congestive heart failure	3030 (6.8)	321 (7.2)	20 (11.6)	171 (7.9)	111 (6.3)	19 (5.6)	2709 (6.8)	92 (10.3)	1224 (7.4)	1120 (6.3)	273 (5.7)	0.259
Reinfarction or stroke	324 (0.7)	37 (0.8)	3 (1.7)	22 (1.0)	8 (0.5)	4 (1.2)	287 (0.7)	12 (1.3)	119 (0.7)	124 (0.7)	32 (0.7)	0.393
Length of stay, days	9 (7, 12)	9 (7, 12)	9 (7, 12)	9 (7, 12)	9 (7, 12)	9 (7, 12)	9 (7, 12)	10 (8, 13)	9 (7, 12)	9 (7, 12)	9 (7, 12)	0.247

ACEI indicates angiotensin-converting enzyme inhibitor; ACHF, ARB, angiotensin receptor blockade; BMI, body mass index; EF, ejection fraction; MACEs, major adverse cardiac events; PCI, percutaneous coronary intervention; and SMuRFs, standard modifiable cardiovascular risk factors.

*The *P* value represented the probability of the difference between the SMuRF-less group (n=4454) and ≥1 SMuRFs group (n=40084).

†Glycated hemoglobin A1c was unavailable for 24318 (54.6%) patients.

‡The baseline and peak troponin T values were unavailable for 31509 (70.7%) and 33615 (75.5%) patients, respectively.

§The baseline and peak troponin I values were unavailable for 14157 (31.8%) and 20047 (45.0%) patients, respectively.

‖The left ventricular EF was unavailable for 8756 (19.7%) patients.

#PCI routes were unavailable for 14065 (39.1%) patients.

**Patients with ≥1 MACE component were counted once.

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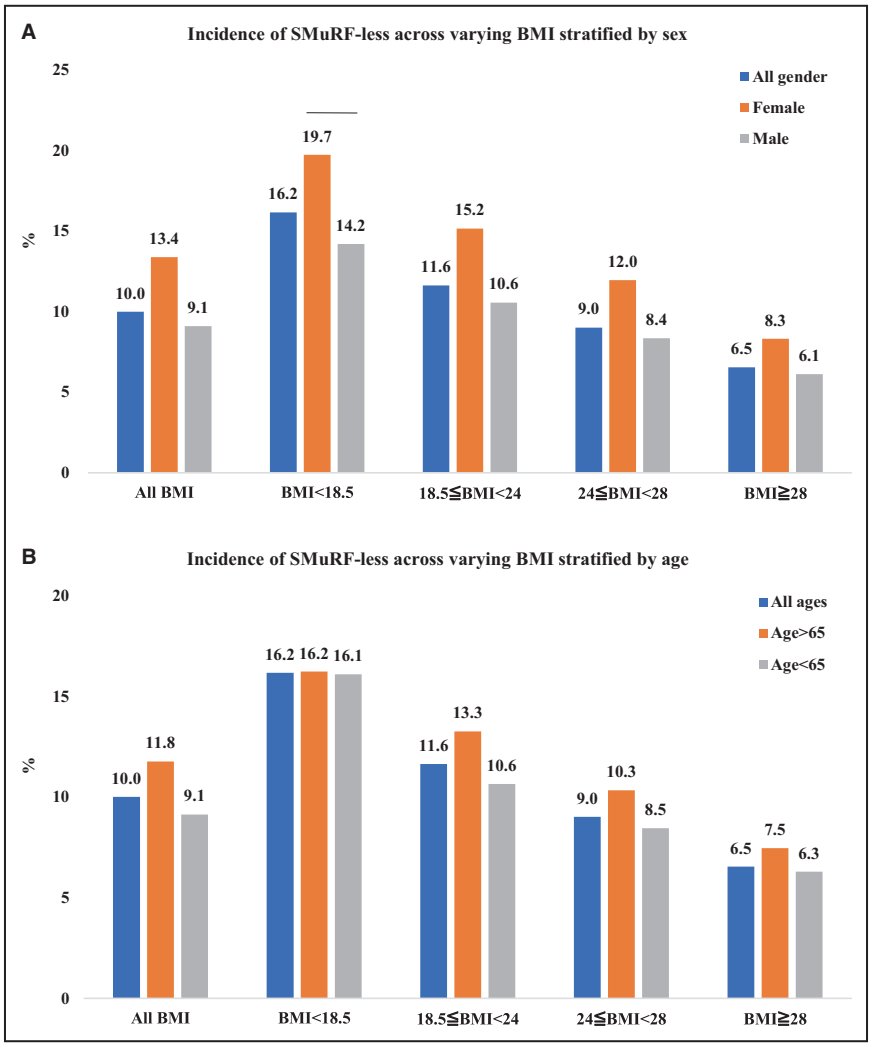

Figure 1. Incidence rate of SMuRF-less status in patients with AMI throughout the BMI spectrum stratified by (A) sex and (B) age.
AMI indicates acute myocardial infarction; BMI, body mass index; and SMuRFs, standard modifiable cardiovascular risk factors.

death (2.1% in the SMuRF-less category and 1.0% in the ≥1 SMuRF category, $P<0.001$) occurred (Table 1).

Table 2 and Table S3 presented the association of SMuRF-less and BMI categories with in-hospital outcomes, respectively. Compared with patients with ≥1 SMuRF, SMuRF-less status significantly correlates with total MACEs and all-cause death under univariate analyses (all $P<0.01$); however, after adjusting for possible covariates, such correlation was observed only with regard to mortality (adjusted OR, 1.750 [95% CI, 1.057–2.896], $P<0.001$). As for BMI, the group with obesity (BMI > 28 kg/m^2) displayed the lowest event rates throughout all outcomes, whereas the group with underweight (BMI<18.5 kg/m^2) showed the highest event rates. Using normal weight (18.5<BMI<24 kg/m^2) as a reference, underweight (BMI<18.5 kg/m^2) linked to a slightly increased risk of incident cardiac shock or acute congestive heart failure (adjusted OR, 1.441 [95% CI, 1.028–2.022], $P=0.034$) (Table S3).

As shown in Figure 2, individuals who were SMuRF-less displayed a higher incidence of mortality or MACEs than patients with at least 1 SMuRF, irrespective of their BMI category. The BMI and all-cause mortality relationship among patients who were SMuRF-less was U shaped, with the concave regions sitting in BMI 24 to 28 kg/m^2 (Figure 2A). In contrast, the MACEs rate decreased roughly linearly as BMI increased in patients with or without SMuRF (Figure 2B). Figure S1 displayed the incidence rate of other in-hospital outcomes (cardiac shock or acute congestive heart failure; reinfarction or stroke) varying SMuRFs-BMI status among patients with AMI. ORs for the association between the SMuRF-BMI status and incident in-hospital outcomes are shown in Table 3 and Table S4. Using ≧1 SMuRF

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Table 2. The Association Between SMuRFs Status or BMI Categories and In-Hospital Outcomes in Multivariate Logistics Regression Analyses

	SMuRFs status		BMI categories			
	≧1 SMuRF (n=40 084)	SMuRF-less (n=4454)	18.5≦BMI<24 (n=18 724)	BMI<18.5 (n=1070)	24≦BMI<28 (n=19 578)	BMI≧28 (n=5166)
All-cause death						
Event (%)	396 (1.0)	95 (2.1)	223 (1.2)	19 (1.8)	217 (1.1)	32 (0.6)
Unadjusted OR (95% CI)	Ref	2.184 (1.742–2.738)	Ref	1.500 (0.935–2.406)	0.930 (0.771–1.122)	0.517 (0.357–0.750)
P value	Ref	<0.001	Ref	0.093	0.448	0.001
Adjusted OR (95% CI)	Ref	1.750 (1.057–2.896)*	Ref	1.105 (0.677–1.802)†	0.776 (0.487–1.238)†	0.727 (0.496–1.067)†
P value	Ref	<0.001	Ref	0.690	0.288	0.103
Major adverse cardiac events						
Event (%)	3105 (7.7)	396 (8.9)	1604 (8.6)	127 (11.9)	1433 (7.3)	337 (6.5)
Unadjusted OR (95% CI)	Ref	1.162 (1.042–1.297)	Ref	1.437 (1.186–1.742)	0.843 (0.783–0.908)	0.745 (0.659–0.841)
P value	Ref	0.007	Ref	<0.001	<0.001	<0.001
Adjusted OR (95% CI)	Ref	1.064 (0.948–1.194)[a]	Ref	1.085 (0.888–1.327)[b]	0.941 (0.826–1.073)[b]	1.093 (0.895–1.334)[b]
P value	Ref	0.294	Ref	0.425	0.364	0.384

BMI indicates body mass index; CAD, coronary artery disease LDL-C, low-density lipoprotein cholesterol; LMCAD, left main coronary artery disease; OR, odds ratio; ref, reference; SMuRFs, standard modifiable cardiovascular risk factors; and STEMI, ST-segment–elevation myocardial infarction.

*Adjusted for demographic factors (age and sex); clinical characteristics (heart rate, diagnosed STEMI, LDL-C, serum creatinine, LMCAD lesion, and multivessel CAD); prehospital pharmacotherapy (antiplatelets and statins); and in-hospital management (intracoronary therapy, dual antiplatelet therapy, and statins).

†Adjusted for demographic factors (age and sex); clinical characteristics (heart rate, diagnosed STEMI, diabetes, hypertension, hypercholesterolemia, current smoking, LDL-C, serum creatinine, LMCAD lesion, and multivessel CAD); prehospital pharmacotherapy (antiplatelets and statins); and in-hospital management (intracoronary therapy, dual antiplatelet therapy, and statins).

and obesity as the reference group, patients who were SMuRF-less or underweight displayed significantly higher mortality risk consistently across all the adjusting models (all $P<0.05$); in particular, the group who were SMuRF-less and underweight exhibited the worst survival with a nearly 3-times increased mortality risk (adjusted OR, 3.854 [95% CI, 2.130–6.973], $P<0.001$). Regarding total MACEs, the risk of the event almost doubled in the group who were SMuRF-less and underweight (unadjusted OR=.109 [95% CI, 1.329–3.346], $P=0.002$); however, such disparity disappeared after adjusting for age and sex (adjusted OR, 1.335 [95% CI, 0.831–2.143], $P=0.232$) (Table 3). Analyses for nonfatal end points showed that none of the SMuRF-BMI subgroups had a higher risk of in-hospital outcomes than the reference group (Table S4).

In Table 4, we conduct subgroup analyses estimating the association between SMuRF-less and in-hospital outcomes stratified by BMI categories; the group with ≧1 SMuRF is the reference within each BMI stratum. Overall, there was a significant risk increment for in-hospital mortality among patients who were SMuRF-less (2.1% versus 1.0%), which was confirmed by multivariable logistic regression analysis, with an adjusted OR of 1.750 (95% CI, 1.057–2.896; $P<0.001$). Moreover, the association of SMuRF-less status with mortality remained robust throughout all BMI categories and cannot be modified by BMI status according to calculated interaction statistics. However, other end points showed no significant association with SMuRF-less status after adjusting for covariates (MACEs: adjusted OR, 1.031 [95% CI, 0.842–0.262]; $P=0.767$; cardiac shock or acute congestive heart failure: adjusted OR, 0.989 [95% CI, 0.795–1.226]; $P=0.909$; reinfarction or stroke: adjusted OR, 0.939 [95% CI, 0.513–1.720]; $P=0.838$), with either no evidence of subgroup significance or interaction due to baseline BMI status (Table 4 and Table S5).

DISCUSSION

This study of large-scale multicenter data from a high-quality national registry is the first to examine the BMI-stratified disparities in the prevalence and prognostic implications of SMuRF-less status among patients hospitalized with first-presentation AMI. We validated the reported SMuRF paradox that patients who have lethal atherosclerosis without adequate attributing risk factors are at higher risk of adverse outcomes. SMuRF-less accompanied by underweight marks the worst survival, whereas the best prognosis was seen in those with the presence of SMuRFs and obesity. Moreover, the SMuRF paradox exists throughout the BMI spectrum and cannot be significantly modified by their baseline BMI status.

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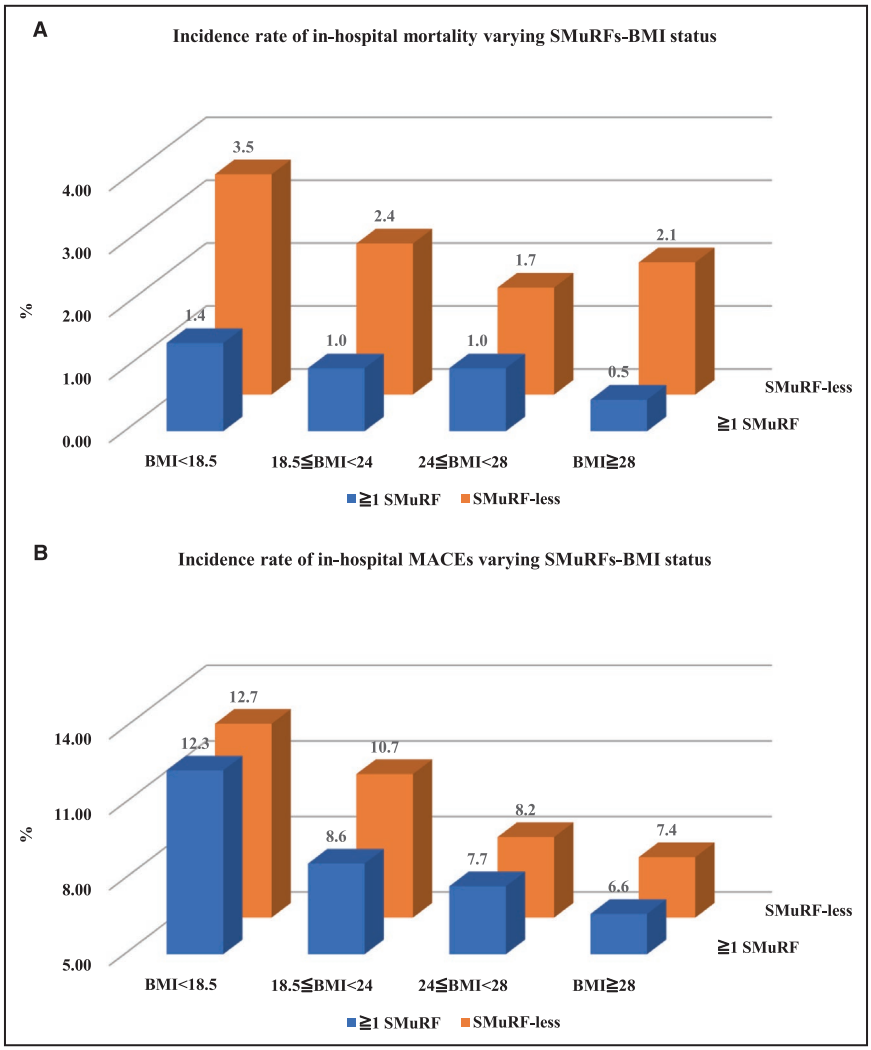

Figure 2. Incidence rate of in-hospital (A) all-cause death and (B) total MACEs in patients with varying SMuRFs-BMI status.
BMI indicates body mass index; MACEs, major adverse cardiovascular events; ref, reference; and SMuRFs, standard modifiable cardiovascular risk factors.

Large epidemiologic studies have revealed that cardiovascular diseases (CVD) remain the globally leading cause of mortality and a significant contributor to disability, and the modifiable risk factors attributed to CVD burden continue to increase to epidemic proportions in the world.[20,21] However, recent studies observed a noticeable proportion of patients who develop AMI despite no evidence of SMuRF and exhibit a higher mortality rate than those with SMuRFs,[22,23] warranting further investigation of potential mechanisms to help guide primary and secondary prevention strategies in this particular patient population. In the present study, 10.0% of patients with first-presentation AMI had no known baseline SMuRF (10.4% in patients with STEMI and 9.0% in patients with non–STEMI), which was higher than previously reported cohorts based on Southeast Asian populations,[9,10] yet much lower than the results from European and American population[6,8,22]; these differences might reflect the worldwide variations exist in CVD risk burden, genetic predisposition, and primary prevention status, etc. Consistent with the SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) study, we observed significantly lower prescriptions of guideline-directed medical therapy and higher mortality risk among patients who were SMuRF-less[22]; however, multivariable analyses showed that this suboptimal guideline-directed medical therapy did not contribute prominently to the increase in MACEs and mortality. To add further information for interpreting the SMuRF paradox from

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Table 3. The Event Rate and Association of SMuRFs-BMI Status With In-Hospital Mortality and MACEs

	Events (%)	Crude model		Model 1*		Model 2†		Model 3‡		Model 4§	
		OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
All-cause death											
≧1 SMuRF and obese (BMI≧28)	25 (0.5)	Ref		Ref		Ref		Ref		Ref	
≧1 SMuRF and overweight (24≦BMI<28)	187 (1.0)	2.038 (1.341–3.098)	0.001	1.786 (1.173–2.270)	0.007	1.759 (1.153–2.685)	0.009	1.751 (1.147–2.673)	0.009	1.749 (0.809–2.628)	0.155
≧1 SMuRF and normal weight (18.5≦BMI<24)	171 (1.0)	2.006 (1.317–3.056)	0.001	1.547 (1.011–2.368)	0.044	1.513 (0.987–2.320)	0.058	1.511 (0.985–2.317)	0.058	1.478 (0.962–2.272)	0.075
≧1 SMuRF and underweight (BMI<18.5)	13 (1.4)	2.825 (1.440–5.544)	0.003	2.047 (1.195–4.213)	0.042	1.961 (1.131–4.129)	0.031	1.915 (1.114–4.013)	0.006	1.718 (1.124–3.784)	0.013
SMuRF-less and obese (BMI≧28)	7 (2.1)	4.063 (1.744–9.463)	0.001	3.903 (1.671–9.117)	0.002	3.815 (1.596–9.121)	0.003	3.540 (1.466–8.547)	0.005	2.939 (1.177–7.339)	0.021
SMuRF-less and overweight (24≦BMI<28)	30 (1.7)	3.322 (1.948–5.664)	<0.001	2.826 (1.645–4.853)	<0.001	2.736 (1.548–4.837)	0.001	3.011 (1.648–5.502)	<0.001	2.828 (1.535–5.210)	0.001
SMuRF-less and normal weight (18.5≦BMI<24)	52 (2.4)	4.699 (2.909–7.592)	<0.001	3.575 (2.182–5.857)	<0.001	3.316 (1–972–5.575)	<0.001	4.162 (1.511–11.461)	0.006	3.625 (1.273–10.323)	0.016
SMuRF-less and underweight (BMI<18.5)	6 (3.5)	6.903 (2.794–17.050)	<0.001	5.220 (2.005–13.587)	0.001	4.572 (1.681–12.436)	0.003	4.206 (2.342–7.551)	<0.001	3.854 (2.130–6.973)	<0.001
MACEs											
≧1 SMuRF and obese (BMI≧28)	319 (6.6)	Ref		Ref		Ref		Ref		Ref	
≧1 SMuRF and overweight (24≦BMI<28)	1365 (7.7)	1.138 (1.001–1.293)	0.048	1.020 (0.896–1.161)	0.767	1.027 (0.901–1.171)	0.689	1.027 (0.900–1.172)	0.691	1.025 (0.898–1.170)	0.711
≧1 SMuRF and normal weight (18.5≦BMI<24)	1430 (8.6)	1.327 (1.169–1.508)	<0.001	1.076 (0.944–1.225)	0.272	1.063 (0.932–1.214)	0.362	1.063 (0.932–1.214)	0.363	1.063 (0.931–1.214)	0.368
≧1 SMuRF and underweight (BMI<18.5)	110 (12.3)	1.919 (1.519–2.424)	<0.001	1.273 (0.994–1.630)	0.056	1.222 (0.947–1.577)	0.122	1.232 (0.955–1.591)	0.109	1.211 (0.666–2.201)	0.531
SMuRF-less and obese (BMI≧28)	25 (7.4)	1.156 (0.757–1.765)	0.502	1.099 (0.716–1.685)	0.666	1.106 (0.713–1.715)	0.652	1.067 (0.686–1.660)	0.773	1.048 (0.672–1.634)	0.836
SMuRF-less and overweight (24≦BMI<28)	144 (8.2)	1.199 (0.972–1.478)	0.090	1.032 (0.834–1.278)	0.771	1.067 (0.851–1.337)	0.576	1.045 (0.830–1.317)	0.202	1.050 (0.833–1.324)	0.680
SMuRF-less and normal weight (18.5≦BMI<24)	220 (10.1)	1.577 (1.315–1.892)	<0.001	1.202 (0.995–1.453)	0.056	1.187 (0.971–1.451)	0.094	1.160 (0.943–1.428)	0.160	1.132 (0.918–1.394)	0.246
SMuRF-less and underweight (BMI<18.5)	22 (12.7)	2.109 (1.329–3.346)	0.002	1.335 (0.831–2.143)	0.232	1.204 (0.735–1.972)	0.088	1.144 (0.696–1.880)	0.596	1.126 (0.683–1.856)	0.642

*Model 1: demographic factors (age and sex).

†Model 2: adjusted for variables in Model 1 plus clinical characteristics (heart rate, diagnosed ST-segment–elevation myocardial infarction, low-density lipoprotein cholesterol, serum creatinine, left main coronary artery disease, and multivessel coronary artery disease).

‡Model 3: adjusted for variables in model 3 plus prehospital pharmacotherapy (antiplatelets and statins).

§Model 4: adjusted for variables in model 3 plus in-hospital management (intracoronary therapy, dual antiplatelet therapy, and statins).

BMI indicates body mass index; MACEs, major adverse cardiac events; OR, odds ratio; ref, reference; and SMuRFs, standard modifiable cardiovascular risk factors.

Table 4. Association Between SMuRF-Less Status and In-Hospital Mortality and MACEs Stratified by BMI Category

	Incidence of events				Association between SMuRF-less and outcomes and its interplay with BMI status					
	Overall, n (%)	SMuRFs-less, n (%)	≥1 SMuRFs, n (%)	*P* value	Unadjusted OR (95%CI)	*P* value	*P* for interaction	Adjusted OR (95%CI)*	*P* value	*P* for interaction
All-cause death										
All BMI categories	491 (1.1)	95 (2.1)	396 (1.0)	<0.001	2.184 (1.742–2.738)	<0.001		1.750 (1.057–2.896)	<0.001	
BMI-stratified										
BMI<18.5	19 (1.8)	6 (3.5)	13 (1.4)	0.127	2.151 (1.704–2.715)	<0.001	0.805	1.715 (1.337–2.200)	<0.001	0.641
18.5≦BMI<24	223 (1.2)	52 (2.4)	171 (1.0)	<0.001	1.995 (1.436–2.773)	<0.001	0.489	1.553 (1.098–2.195)	0.013	0.355
24≦BMI<28	217 (1.1)	30 (1.7)	187 (1.0)	0.013	1.630 (1.105–2.404)	0.014	0.263	2.077 (1.543–2.794)	<0.001	0.067
BMI≧28	217 (1.1)	30 (1.7)	187 (1.0)	0.013	2.054 (1.625–2.598)	<0.001	0.128	1.658 (1.290–2.130)	<0.001	0.184
MACEs										
All BMI categories	3501 (7.9)	396 (8.9)	3105 (7.7)	0.007	1.162 (1.042–1.297)	0.007		1.031 (0.842–1.262)	0.767	
BMI-stratified										
BMI<18.5	127 (11.9)	22 (12.7)	105 (11.7)	0.707	1.155 (1.032–1.292)	0.012	0.848	1.065 (0.946–1.199)	0.297	0.816
18.5≦BMI＜24	127 (11.9)	22 (12.7)	105 (11.7)	0.707	1.106 (0.943–1.297)	0.215	0.523	1.010 (0.856–1.192)	0.903	0.418
24≦BMI<28	1433 (7.3)	135 (7.6)	1298 (7.3)	0.578	1.054 (0.876–1.267)	0.578	0.218	1.105 (0.958–1.275)	0.171	0.356
BMI≧28	337 (6.5)	25 (7.4)	312 (6.5)	0.501	1.151 (1.028–1.290)	0.015	0.986	1.061 (0.942–1.196)	0.329	0.968

BMI indicates body mass index; MACEs, major adverse cardiac events; OR, odds ratio; and SMuRFs, standard modifiable cardiovascular risk factors.

*Adjusted for demographic factors (age and sex); clinical characteristics (heart rate, diagnosed ST-segment–elevation myocardial infarction, low-density lipoprotein cholesterol, serum creatinine, left main coronary artery disease, and multivessel coronary artery disease); prehospital pharmacotherapy (antiplatelets and statins); and in-hospital management (intracoronary therapy, dual antiplatelet therapy, and statins).

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the perspective of BMI, we thoroughly examined the combined effect and interplay of BMI-SMuRF status among patients with AMI.

The prevalence of patients with underweight and overweight represents significant global and national public health burdens.[24,25] The exact effect of different degrees of BMI on cardiovascular and overall prognosis are areas of debate and great concern.[24–26] As it typically correlates with sarcopenia, poverty, and infection, underweight generally presents with a poorer quality of life with an increased likelihood of a higher risk of developing frailty, disability, and mortality, especially among those with various chronic complications and diseases and in aging.[27–29] As China continues to modernize and become more urbanized, the prevalence of being underweight has decreased drastically over the past 30 years from 10% to 20% to 3% to 6%; however, it is still a severe issue in rural areas, especially among older residents.[30] Meanwhile, along with the increased trend of dietary richness and sedentary behavior, the Chinese population with obesity more than tripled during the past 2 decades, with an average BMI rising from 23 kg/m^2 to 24 kg/m^2.[31] Studies over the past decade have demonstrated a strong obesity paradox, suggesting that patients with CVDs who are overweight or obese often have a better prognosis than leaner patients with similar diagnoses.[32–34] An extensive meta-analysis evaluated the risk of all-cause mortality across varying BMI, which turned out that optimal survival occurred in the group with BMI ranging from 25 to 30 kg/m^2.[35] Data from the ORIGIN (Outcome Reduction With Initial Glargine Intervention) trial found that compared with the reference group of participants with a BMI of between 22 and 24.9 kg/m^2, all-cause mortality risk was lower in those with a BMI of 25 to 39.9 kg/m^2, whereas it was elevated 29% to 35% in those with baseline BMIs <22 kg/m^2.[36] The potential biological mechanisms underlying the survival advantage of higher BMI in patients with established CVD have yet to be fully elucidated, which may include theories involving higher muscle reserves and the increased size of metabolically healthy adipose tissue.[37–39] To be more specific, healthy perivascular adipose tissue may play a role in preventing the development of atherosclerosis, it stores and combusts lipids, releases multiple vasoactive molecules (ie, nitric oxide, hydrogen sulfide, adiponectin, etc.), and downregulates the inflammatory microenvironment to promote vascular health.[40,41]

Data from the present study presented an apparent decline in total MACEs rate as BMI increases across the spectrum, which accorded with the obesity paradox. Regarding the mortality outcome, whereas the optimal survival BMI interval seemed to differ between patients with and without SMuRFs, those with overweight or obesity (BMI>24 kg/m^2) were still linked to better survival than those who were leaner. These results indicated that the obesity paradox can occur regardless of the presence or absence of a deteriorated metabolic profile (impaired glucose tolerance, plasma levels of lipids, blood pressure, etc.) among patients with AMI. Given observations of this study, those in the lowest BMI group were among the oldest and had the lowest prescription of guideline-directed medical therapy, indicating that age-related changes in body fat distribution, sarcopenia, and malnutrition, as well as the underuse of evidence-based pharmacotherapy, may be clues to the obesity paradox, and these factors may outweigh the metabolic components when affecting outcomes. Nonetheless, a prominent selection bias must be considered when interpreting the obesity paradox in a cohort that includes only patients with AMI. To be specific, patients without overweight who nevertheless develop AMI may indicate their more substantial inherited susceptibility to relevant diseases compared with those obese; thus, it is reasonable to observe that patients with obesity who got AMI are less susceptible to MACEs than those without overweight or obesity. In subgroup analysis, SMuRF-less status remained a harmful sign across the BMI categories; however, interaction analyses provided no evidence that BMI significantly modifies the association of SMuRF-less status with in-hospital mortality and other end points, suggesting that lower BMI was not the main driving force of the SMuRF paradox. The populations who are SMuRF-less are an easily overlooked group due to the absence of noticeable CVD risk factors. However, their tendency to develop AMI despite having no prominent risk burden generally suggests their more substantial individual susceptibility to atherosclerotic disease, which makes this kind of neglect a concerning problem. Data in this study highlight the need for increased awareness and identification of the population who are SMuRF-less in AMI care, regardless of BMI, which can facilitate guiding post-AMI prevention. As we move toward more individualized and precise AMI care, studies investigating the explanations of the SMuRF paradox are an unmet need to aid risk stratification and effective secondary prevention strategies. Clinicians must remain vigilant in identifying the various SMuRF-BMI phenotypes, particularly in the at-risk population.

To the best of our knowledge, the present study is the first large-scale analysis investigating whether the SMuRF paradox is influenced by baseline BMI status among patients with AMI using a comprehensive nationwide inpatient data set. However, we are aware of several limitations. As an observational study, we could not impute direct causality or account for other potential residual confounding factors. Although several other CVD risk factors or biomarkers were examined, data were lacking on some covariates (eg, family history of

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premature coronary artery disease, lipoprotein(a), malignancy); besides, information on socioeconomic or psychosocial status was missing. In addition, the proportion of male patients in our cohort was as high as 79.1%, thus the results should be interpreted cautiously in the female population. Because only in-hospital data were available, we could not access the postdischarge or long-term survival information, and analyses about the potential time-dependent effects were not applicable. What also needs to be noted is that patients with substantial levels of obesity (BMI>35 kg/m^2) account for only 0.4% (n=180) of the total participants and thus have not been analyzed separately, data on the association between extreme obesity and outcomes in patients with AMI still need further examination in larger data sets. Moreover, as they are based on Chinese people, the results should be carefully interpreted and extended to other ethnicities.

CONCLUSIONS

In a nationwide registry of patients with first-presentation AMI in China, approximately one tenth had no SMuRF, more frequently women, older people, and underweight. Compared with those with at least 1 SMuRF, patients who were SMuRF-less have a significantly higher risk of in-hospital mortality irrespective of their BMI categories, whereas in-hospital survival was the most favorable among patients with ≥1 SMuRF and obesity.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Data S1
Tables S1–S6
Figure S1

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