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Mortality in ST-segment elevation myocardial infarction patients without standard modifiable risk factors: A race disaggregated analysis

Saadiq M. Moledina [a,1], Ofer Kobo [b,1], Hammad Lakhani [a], Abhishek Abhishek [c], Purvi Parwani [d], Annabelle Santos Volgman [e], Rachel M. Bond [f], Muhammad Rashid [a], Gemma A. Figtree [g], Mamas A. Mamas [a,h,*]

[a] Keele Cardiovascular Research Group, Centre for Prognosis Research, Institute for Primary Care and Health Sciences, Keele University, United Kingdom
[b] Department of Cardiology, Hillel Yaffe Medical Centre, Hadera, Israel
[c] Nottingham City Hospital, Nottingham, United Kingdom
[d] Division of Cardiology, Department of Medicine, Loma Linda University Health, Loma Linda, CA, USA
[e] Division of Cardiology, Rush University Medical Center, Chicago, IL, USA
[f] Women's Heart Health, Dignity Health, Gilbert, AZ, USA
[g] Kolling Institute, Royal North Shore Hospital and Faculty of Medicine and Health, University of Sydney, Australia
[h] Department of Cardiology, Jefferson University, Philadelphia, USA

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ABSTRACT

Background: Individuals who present with STEMI without the standard cardiovascular risk factors (SMuRFs) of diabetes, hypercholesterolemia, hypertension, and smoking, coined SMuRF-less are not uncommon. Little is known about their outcomes as a cohort and how they differ by race.

Methods & Results: We identified 431,615 admissions with STEMI in the National Inpatient Sample (NIS) database 2015–2018, including patients with ≥ 1 SMuRF (n = 369,870) and those who were SMuRF-less (n = 234,745). SMuRF-less patients presented at a similar age (median age 63y vs 63y), were less likely to be female (33.6 % vs 34.6 %) and were almost twice as likely to present as a cardiac arrest (13.7 % vs 7.0 %), than those with ≥ 1 SMuRFs. SMuRF-less patients were less frequently in receipt of ICA (71.3 % vs 83.8 %) and PCI (58.0 % vs 72.2 %) compared to those with ≥ 1 SMuRF. Our race disaggregated analysis showed ethnic minority SMuRF-less patients were less likely than White patients to receive ICA and PCI, which was most apparent in Black patients with reduced odds of ICA (OR: 0.47, 95 % CI: 0.43–0.52) and PCI (OR: 0.46, 95 % CI: 0.52–0.50). Similarly, in ethnic minority subgroups within the SMuRF-less cohort, mortality and MACCE were significantly higher than in White patients. This was most profound in Black patients with in-hospital mortality (OR: 1.90, 95 % CI: 1.72–2.09) and MACCE (OR: 1.63, 95 % CI: 1.49–1.78) compared to White patients.

Conclusion: Ethnic Minority SMuRF-less patients were less likely than White SMuRF-less patients to receive ICA and PCI and had worse mortality outcomes.

1. Introduction

Whilst the well-known modifiable risk factors remain essential public health targets to reduce the burden of myocardial infarction (MI), individuals who present with ST-segment elevation myocardial infarction (STEMI) without the standard cardiovascular risk factors (SMuRFs) of diabetes, hypercholesterolemia, hypertension and smoking are not uncommon and represent up to 30 % of the STEMI population[1–3]. They have been shown to have a significantly increased risk of all-cause early mortality (<30 days) compared to patients with a least one SMuRF [1], an observation that was partially mediated by lower rates of guideline-based therapies[1].

In the United States (US), ethnic minorities with STEMI represent a heterogeneous group of patients who tend to present at a younger age, have been shown to have an increased burden of coronary artery disease (CAD) with a higher prevalence of diabetes, hypercholesterolemia and hypertension[4,5]. However, the proportion of SMuRF-less individuals in the ethnic minority STEMI cohort, their clinical characteristics, the

* Corresponding author at: Keele Cardiovascular Research Group, Centre for Prognosis Research, Keele University, Stoke-on-Trent, UK.
E-mail address: mamasmamas1@yahoo.co.uk (M.A. Mamas).
[1] Authors contributed equally.

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quality of their care, and their outcomes are not known.

Thus, using data from a large nationwide database, with greater than 430,000 STEMI patients from the National Inpatient Sample (NIS) database (2015–18), we examined the characteristics, management strategies, quality of care and outcomes of patients without SMuRFs by race.

2. Methods:

2.1. Data source

The National Inpatient Sample (NIS) is the largest all-payer inpatient health care database in the US, developed by the Healthcare Cost and Utilization Project (HCUP) and sponsored by the Agency for Healthcare Research and Quality (AHRQ)[6]. The NIS dataset contains hospital information on about 7 to 8 million yearly hospital discharges beginning in 2004. Since 2012, the NIS collects information on discharges from all hospitals participating in HCUP, approximating a 20 % stratified sample of all discharges from US community hospitals.

2.2. Study design and population

We analysed all adult (≥18 years) patients hospitalized for STEMI from 1st October 2015 through December 2018. This period was chosen due to the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes implemented in October 2015 which would provide more granular data than the previous ICD-9 coding. Patient and procedural characteristics were extracted using ICD-10 codes provided in Table S1. According to zip codes, patient demographics were recorded for each hospital discharge, including age, gender, race, admission day (weekday or weekend), expected primary payer, and median household income. Missing records for age, gender, race, elective and weekend admission, and mortality status were excluded from the analysis. Patients with previous percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG) surgery, myocardial infarction (MI), or elective admissions were also excluded from the analysis (Fig. 1 for study flow diagram). Each discharge record had information on up to 40 diagnoses. A complete list of ICD 10-CM codes used to identify SMuRFs is provided in Supplementary Table 1. SMuRFs included current smoking, diabetes, hypertension, and hypercholesterolemia. ICD 10-CM codes were also used to identify complications and procedural information during hospitalization, including invasive coronary angiography (ICA), PCI, CABG surgery, thrombolysis, use of mechanical ventilation, ventricular assist device, or intra-aortic balloon pump (IABP).

2.3. Outcomes

The main outcomes measured were in-hospital adverse events, stratified by the presence of at least one SMuRF vs no SMuRFs. Main outcomes included major adverse cardiovascular and cerebrovascular events (MACCE), all-cause mortality, acute ischemic cerebrovascular accident (CVA), and major bleeding. MACCE was defined as a composite of all-cause mortality, acute ischemic CVA or transient ischemic attack, and cardiac complications. Cardiac complications included coronary artery dissection, pericardial effusion (including tamponade), Dressler's syndrome, post-MI angina, intracardiac thrombus, reinfarction, and acute mechanical complications. Major bleeding events were defined as a composite of gastrointestinal, retroperitoneal, intracranial, and intracerebral haemorrhage, periprocedural haemorrhage, unspecified haemorrhage, or the requirement for blood transfusions. Receipt of invasive management procedures such as ICA, PCI, and CABG surgery was also recorded, as was the discharge destination.

2.4. Statistical analysis

Continuous variables are presented as a median and interquartile range due to skewed data, and categorical data are presented as frequencies and percentages. Categorical variables were compared using Pearson's chi-square test, while continuous variables were compared using the Kruskal Wallis test. Sampling weights were used to calculate the estimated total discharges as specified by AHRQ. Multivariable logistic regression models were used to examine the association between in-hospital outcomes and procedures and presence of any SMuRF among the entire cohort and White vs ethnic minorities (grouped as Black, Hispanic, and Mixed (Other - Asian/Pacific Islander, Native American

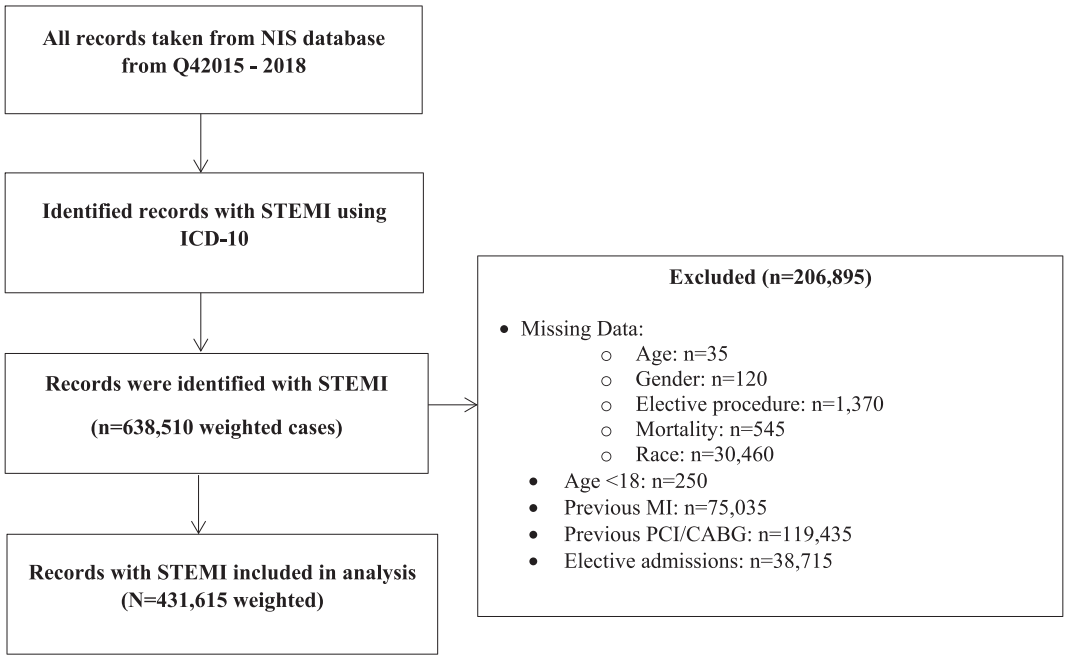

Fig. 1. Flow diagram of study population. STEMI; ST-segment myocardial infarction, ICD; International Classification of Disease, PCI; percutaneous coronary intervention, CABG; coronary artery bypass grafting surgery, MI; myocardial infarction.

Table 1
Demographics, record characteristics and comorbidities of patients, by presence of SMuRFs.

	SMuRF-less	≥ 1 SMuRFs	P value
Number of weighted records	34,745 (8 %)	396,870 (92 %)	
Age (years), median (IQR)	63 (53,75)	63 (54,73)	<0.001
Females, %	33.6 %	34.6 %	<0.001
Ethnicity			<0.001
White	77.3 %	75.6 %	
Black	7.9 %	10.2 %	
Hispanic	7.5 %	7.6 %	
Other	7.4 %	6.5 %	
Record Characteristics			
Anterior STEMI	34.6 %	33.8 %	0.002
Cardiac Arrest	13.2 %	7 %	<0.001
Ventricular Fibrillation	13.5 %	7.7 %	<0.001
Ventricular tachycardia	14.1 %	11.1 %	<0.001
Cardiogenic Shock	19.4 %	12.7 %	<0.001
Length of stay, days, median (IQR)	3 (2,6)	3 (2,5)	<0.001
Total charge, $, median (IQR)	77,630 (45,110, 141,273)	78,529 (50,747, 126,009)	<0.001
Comorbidities			
Cerebrovascular disease	1.6 %	3 %	<0.001
Heart failure	22.5 %	25.1 %	<0.001
Valvular disease	6.4 %	8.9 %	<0.001
Atrial fibrillation/flutter	15.4 %	16 %	0.007
Peripheral vascular disease	2.6 %	5.5 %	<0.001
Chronic lung disease	9.3 %	16.3 %	<0.001
Chronic renal failure	5 %	14.3 %	<0.001
Obesity	5.7 %	15.7 %	<0.001
Anaemia	18.2 %	17.5 %	<0.001
Thrombocytopenia	6.5 %	4.8 %	<0.001
Coagulopathy	4.7 %	2.1 %	<0.001
Dementia	5.3 %	4.5 %	<0.001
Chronic Liver Disease	0.5 %	0.5 %	0.691
Homelessness	0.3 %	0.2 %	0.63
Solid malignancy	3.3 %	2.4 %	<0.001
Hematologic Malignancies	1.4 %	0.9 %	<0.001
Metastatic cancer	2.1 %	1.2 %	<0.001
Management			
Coronary Angiography	71.3 %	83.8 %	<0.001
PCI	58 %	72.2 %	<0.001
CABG	3.2 %	5.1 %	<0.001
Thrombolysis	0.5 %	0.5 %	0.245

SMuRF; standard cardiovascular modifiable risk factor, IQR; interquartile range, PCI; percutaneous coronary intervention, CABG; coronary artery bypass grafting surgery, MI; myocardial infarction, IABP; intra-aortic balloon pump, LV; left ventricle, ECMO; extracorporeal membrane oxygenation.

and Other non-White ethnic minority groups), expressed as odds ratios (OR) with corresponding 95 % confidence intervals (CI). All models were adjusted for baseline differences between the groups, controlling for the following covariates: age, gender, weekend admission, hospital bed size, region and location/teaching status, cardiogenic shock, ventricular fibrillation (VF), ventricular tachycardia (VT), atrial fibrillation (AF), heart failure (HF), hypertension, dyslipidaemias, diabetes mellitus, valvular heart disease, peripheral vascular disease (PVD), smoking status, chronic lung disease, chronic liver disease, anaemia, obesity, thrombocytopenia, coagulopathies, malignancies, dementia, and for outcomes models, ICA PCI, and CABG surgery were also included.

All statistical analyses were performed on IBM SPSS version 26. Statistical significance was set at the 2-tailed 0.05 level, without multiplicity adjustment.

3. Results:

3.1. Baseline characteristics

Between October 2015 to December 2018, 638,510 patients were admitted to US hospitals and, during the hospitalization, received a diagnosis of STEMI. Applying relevant exclusion criteria (Fig. 1) produced a study cohort of 431,615 (32 % excluded). Of these, 34,745 (8 %) had no SMuRFs. Differences in clinical characteristics at admission between the two groups are presented in Table 1. Patients without SMuRFs presented at a similar age (median age 63 years vs 63 years), were less likely to be female (33.6 % vs 34.6 %, P < 0.001) and more likely to be White (77.3 % vs 75.6, P < 0.001) than those with ≥ 1 SMuRFs. They were almost twice as likely to present as a cardiac arrest (13.7 % vs 7.0 %, P < 0.001), and had higher rates of cardiogenic shock (19.4 % vs 12.7 %, P < 0.001), VT (14.1 % vs 11.1 %, P < 0.001) and VF (13.5 % vs 7.7 %, P < 0.001). SMuRF-less patients were less frequently comorbid with obesity (5.7 % vs 15.7 %, P < 0.001), but more frequently diagnosed with solid malignancies (3.3 % vs 2.4 %, P < 0.001) or metastatic cancer (2.1 % vs 1.2 %, P < 0.001). They were less frequently in receipt of ICA (71.3 % vs 83.8 %, P < 0.001), PCI (58.0 % vs 72.2 %, P < 0.001), or CABG surgery (3.2 % vs 5.1 %, P < 0.001), but more frequently received circulatory support (14.0 % vs 9.3 %, P < 0.001) or mechanical ventilation (26.1 % vs 13.3 %, P < 0.001) than patients with ≥ 1 SMuRFs.

Unadjusted outcomes of patients stratified by SMuRF status are shown in Table 2. SMuRF-less patients had significantly higher rates of mortality (23.2 % vs 10.2 %, P < 0.001), MACCE (29 % vs 15 %, P < 0.001), acute ischemic CVA (3.8 % vs 2.4 %, P < 0.001), cardiac complications (5.7 % vs 3.8 %, P < 0.001) and major bleeding (6.8 % vs 4.2 %, P < 0.001) than those with ≥ 1 SMuRFs.

After adjusting for baseline characteristics and management strategy, SMuRF-less patients were less likely to receive ICA (OR: 0.69, 95 % CI: 0.67–0.71) or PCI (0.65, 95 % CI: 0.63–0.67) but were more likely to receive CABG surgery (OR: 1.20, 95 % CI: 1.11–1.29). They had increased risk of MACCE (OR: 1.36, 95 % CI: 1.31–1.42), mortality (OR: 1.44, 95 % CI: 1.38–1.51), CVA (OR: 1.38, 95 % CI: 1.28–1.51) or cardiac complications (OR: 1.28, 95 % CI: 1.20–1.36) compared to those with ≥ 1 SMuRF (Table 3).

3.2. Race-disaggregated analysis

Differences in clinical characteristics of patients by SMuRF status and race are shown in Table 4. In the cohort of patients with ≥ 1 SMuRF, all ethnic minority groups tended to present younger than White patients by an average of between 2 and 4 years. Hispanic patients (29.7 %) and

Table 2
In hospital outcomes, stratified by presence of SMuRFs.

	SMuRF-less	≥ 1 SMuRF	P value
Number of weighted records	34,745 (8 %)	396,870 (92 %)	
MACCE[1]	29 %	15 %	<0.001
Mortality	23.2 %	10.2 %	<0.001
Acute Ischemic CVA	3.8 %	2.4 %	<0.001
Cardiac Complications	5.7 %	3.8 %	<0.001
Coronary artery dissection	2 %	1 %	<0.001
Pericardial effusion (including tamponade)	2.1 %	1.1 %	<0.001
Tamponade	0.6 %	0.3 %	<0.001
Dressler's syndrome	0.4 %	0.4 %	0.07
Post MI angina	0.4 %	0.6 %	<0.001
Intracardiac thrombus	0.6 %	0.4 %	<0.001
Mechanical complications[2]	0.7 %	0.3 %	<0.001
Vascular complications	0.2 %	0.2 %	0.503
Major Bleeding	6.8 %	4.2 %	<0.001
GI bleed	4 %	2.4 %	<0.001
Procedural related bleeding	1.2 %	1 %	0.001
Retroperitoneal Bleed	0.4 %	0.2 %	<0.001
Intracranial Hemorrhage	1.4 %	0.6 %	<0.001
Post-procedural shock	0.7 %	0.4 %	<0.001

SMuRF; standard cardiovascular modifiable risk factor, MACCE; major adverse cardiovascular and cerebrovascular events, CVA; cerebrovascular accident; MI – myocardial infarction; GI - gastrointestinal.

Table 3
Adjusted OR of SMuRF-less patients for In-Hospital procedures and outcomes compared to patients with ≥ 1 SMuRF.

	All population	
	OR (95 %CI)	P Value
Coronary Angiography*	0.69 (0.67–0.71)	<0.001
PCI*	0.65 (0.63–0.67)	<0.001
CABG*	1.2 (1.11–1.29)	<0.001
MACCE**	1.36 (1.31–1.42)	<0.001
Mortality **	1.44 (1.38–1.51)	<0.001
CVA**	1.38 (1.28–1.51)	<0.001
Major Bleeding**	1.02 (0.96–1.8)	0.5

SMuRF; standard cardiovascular modifiable risk factor; PCI – percutaneous coronary intervention, CABG- coronary artery bypass graft, MACCE; major adverse cardiovascular and cerebrovascular events, CVA; cerebrovascular accident.
*Reference: SMuRF ≥ 1 Adjusted for age, gender, weekend admission, Hospital bed size, region and location/teaching status, ST elevation myocardial infarction, cardiogenic shock, ventricular fibrillation, ventricular tachycardia, atrial fibrillation, heart failure, hypertension, dyslipidaemias, diabetes mellitus, valvular heart disease, smoking status, chronic lung disease, chronic liver disease, anaemia, thrombocytopenia, coagulopathies, malignancies, dementia.
**Reference: SMuRF. Adjusted for age, gender, weekend admission, Hospital bed size, region and location/teaching status, cardiogenic shock, cardiogenic shock, ventricular fibrillation, ventricular tachycardia, atrial fibrillation, heart failure, hypertension, dyslipidaemias, diabetes mellitus, valvular heart disease, peripheral vascular disease, smoking status, chronic lung disease, chronic liver disease, anaemia, obesity, thrombocytopenia, coagulopathies, malignancies, dementia, coronary angiography, PCI, CABG.

Mixed patients (27.6 %) were less frequently female than White patients (34.9 %), whilst Black patients were more frequently female (40.6 %). Black, Hispanic, and Mixed patients more frequently presented as a cardiac arrest than White patients (8.9 % vs 7.2 % vs 6.9 % vs 6.7 %). Black and Hispanic patients were less frequently in receipt of ICA (77.5 %% vs 84.1 % vs 84.5 %) than White patients. Black, Hispanic and Mixed patients were less frequently in receipt of PCI (63.1 % vs 71.7 % vs 71.8 %) than White patients (73.5 %). In the SMuRF-less cohort, all ethnic minority groups tended to present younger than White patients by an average of 7 years. Hispanic patients (29.3 %) and Mixed patients (26.8 %) were less frequently female than White patients (34.4 %), whilst Black patients were more frequently female (36.2 %). Black (20.7 %) and Mixed (14.5 %) patients more frequently presented as a cardiac arrest than White patients (12.5 %). Black and Hispanic patients were less frequently in receipt of ICA (61.4 % vs 69.4 % vs 72.2 %), PCI (42.6 % vs 53.9 % vs 59.5 %) and CABG surgery (2.2 % vs 1.7 % vs 3.6 %) compared to White patients.

Differences of in-hospital outcomes of patients by SMuRF status and race are shown in Table 5. In the cohort of patients with ≥ 1 SMuRF, all ethnic minority patients had a higher frequency of mortality and MACCE than White patients. This difference was most pronounced in Black patients with increased frequency of mortality (12.2 % vs 9.8 %) and MACCE (18.7 % vs 14.4 %) compared to White patients. In the SMuRF-less cohort, MACCE was more frequent in all ethnic minority subgroups (Black: 31.4 %, Hispanic 28.7 %, Mixed: 31.6 %) compared to White patients (27.9 %). Mortality was more frequent for Black (31.4 %) and Mixed (26.4 %) patients in comparison to White (22.2 %) patients.

Table 6 shows the adjusted odds of SMuRF-less ethnic minorities for in-hospital procedures and outcomes. Whilst all ethnic minority SMuRF-less patients were less likely than White patients to receive ICA and PCI, this was most apparent in Black patients with the reduced odds of ICA (OR: 0.47, 95 % CI: 0.43–0.52) and PCI (OR: 0.46, 95 % CI: 0.52–0.50). Similarly, in all the individual ethnic minority subgroups within the SMuRF-less cohort, mortality and MACCE were significantly higher than in White patients. This finding was most profound in Black patients with in-hospital mortality (OR: 1.90, 95 % CI: 1.72–2.09) and MACCE (OR: 1.63, 95 % CI: 1.49–1.78) compared to White patients.

Table 7 shows the adjusted odds of SMuRF-less patients compared to patients with ≥ 1 SMuRF by their race. Whilst all ethnicities were less likely to receive ICA and PCI in their SMuRF-less cohort, the odds were more pronounced in Black (ICA – (OR: 0.62, 95 % CI: 0.56–0.70), PCI – (OR: 0.59, 95 % CI: 0.53–0.65)) and Hispanic patients (ICA – (OR: 0.56, 95 % CI: 0.49–0.63), PCI – (OR: 0.48, 95 % CI: 0.43–0.53)) compared to White patients (ICA – (OR: 0.75, 95 % CI: 0.72–0.78), PCI – (OR: 0.70, 95 % CI: 0.68–0.73)). The odds of MACCE were similar in magnitude in Hispanic (OR: 1.44, 95 % CI: 1.26–1.65) and Mixed (OR: 1.69, 95 % CI: 1.47–1.95) patients compared to White (OR: 1.38, 95 % CI: 1.32–1.44) patients. Similarly, the odds of mortality were similar in Hispanic (OR: 1.52, 95 % CI: 1.29–1.59) and Mixed (OR: 1.86, 95 % CI: 1.58–2.20) patients compared to White patients (OR: 1.45, 95 % CI: 1.38–1.53).

Supplement table 2 shows the demographics and clinical characteristics of SMuRF-less patient vs those with ≥ 1 SMuRF by their individual races. Ethnic minority SMuRF-less patient presented 2–4 years younger on average than those with ≥ 1 SMuRF. Supplementary Fig. 1 shows the percentage of SMuRF-less patients by individual race.

Our key findings are presented in the key central illustration figure (Fig. 2).

4. Discussion:

The results of this analysis of more than 430,000 patients hospitalised with STEMI reveal several important findings. After excluding patients with a known history of CAD, almost one in ten patients hospitalised with STEMI had no SMuRFs. Such SMuRF-less patients with STEMI typically were more frequently White, female and less comorbid. SMuRF-less patients were more likely to have cardiac arrest at presentation and were more likely to require circulatory support and mechanical ventilation. Following adjustment for baseline characteristics and management strategies, patients without SMuRFs had increased in-hospital mortality and in-hospital MACCE. Our race-disaggregated analysis showed that there was significant variability in the frequency of presentation of SMuRF-less STEMI patients by race. Ethnic minority patients were significantly younger at presentation, less likely to be female, present with AF and valvular disease, and more likely to present with cardiac arrest than White patients. Following adjustment for baseline characteristics and management strategies, Black and Hispanic patients without SMuRFs were significantly less likely to receive ICA, PCI, or CABG surgery. They had higher rates of in-hospital mortality, MACCE, and major bleeding compared to White patients without SMuRFs.

Prior studies that have looked at the outcomes of STEMI patients according to race have important limitations. The burden of CAD is significantly higher in ethnic minority populations, with South Asian patients having the highest burden of diabetes and Black patients with the highest frequency of hypertension[7]. Suboptimal care processes and inferior outcomes in this population have been linked to phenotypical differences and socioeconomic factors. Our study is the first race-disaggregated analysis to look at the outcomes of STEMI patients without the classical SMuRFs[8].

Our analysis shows that in STEMI patients without SMuRFs, the outcomes of mortality and MACCE were significantly worse compared to those with at least one SMuRF. This is confirmatory of the findings by Figtree et al, who, in their multicentre study using the SWEDEHEART database, found that patients without SMuRFs had increased mortality compared to those with conventional risk factors. Whilst the cause of this is largely unknown, potential mechanisms to explain the increased mortality of SMuRF-less patients presenting with STEMI has included increased rates of life-threatening arrhythmias with greater frequency of presentations as a cardiac arrest[1]. Interestingly, our previous work has shown that in non-ST segment myocardial infarction (NSTEMI), outcomes of mortality and MACCE were better in those without any SMuRFs compared to those who had at least one modifiable risk factor, likely highlighting differences in pathogeneses between STEMI and

Table 4
Demographics, record characteristics, comorbidities, and in-hospital procedures of patients with and without SMuRF, by race.

	≥ 1 SMuRF					SMuRF-less				
	Whiten-300,190 (75.6 %)	Black n- 40,610 (10.2 %)	Hispanic n-30,135 (7.6 %)	Other n-25,935 (6.5 %)	P value	White n-26,855 (77.3 %)	Blackn-2,735 (7.8 %)	Hispanic n-2,595 (7.4 %)	Other n-2,560 (7.4 %)	P value
Age (years), median (IQR)	64 (55,74)	60 (52,69)	61 (52,72)	62 (53,72)	<0.001	65 (55,75)	58 (45,67)	58 (46,69)	58 (49,69)	<0.001
Females, %	34.9 %	40.6 %	29.7 %	27.6 %	<0.001	34.4 %	36.2 %	29.3 %	26.8 %	<0.001
Record Characteristics										
Anterior STEMI	33.6 %	32.1 %	34.7 %	38.1 %	<0.001	34.6 %	26.5 %	34.3 %	43.6 %	<0.001
Cardiac Arrest	6.7 %	8.9 %	7.2 %	6.9 %	<0.001	12.4 %	20.7 %	12.5 %	14.5 %	<0.001
Ventricular Fibrillation	7.9 %	8 %	6.5 %	6.6 %	<0.001	13.5 %	14.8 %	10 %	16.2 %	<0.001
Ventricular tachycardia	11.5 %	10.1 %	9.5 %	9.7 %	<0.001	14.4 %	13.7 %	10.6 %	15.4 %	<0.001
Cardiogenic Shock	12.6 %	11.4 %	13.4 %	15 %	<0.001	19 %	21.8 %	15.8 %	24.8 %	<0.001
Length of stay, days, median (IQR)	3 (2,5)	3 (2,6)	3 (2,5)	3 (2,5)	<0.001	3 (2,6)	4 (2,10)	2 (2,5)	3 (2,6)	<0.001
Total charge, $, median (IQR)	76,322 (50,169, 120,718)	75,116 (46,133, 124,646)	101,200 (63,795, 161,548)	89,126 (56,104, 149,238)	<0.001	75,371 (44,370, 135,636)	83,065 (44,445, 180,458)	89,954 (48,124, 151,639)	86,225 (49,107, 164,042)	<0.001
Comorbidities										
Cerebrovascular disease	2.8 %	4.8 %	2.8 %	2.8 %	<0.001	1.5 %	2.4 %	2.1 %	1.2 %	<0.001
Heart failure	24.3 %	28.8 %	26.3 %	27.6 %	<0.001	23 %	23.8 %	16.4 %	22.9 %	<0.001
Valvular disease	9.2 %	8.2 %	7.5 %	8.4 %	<0.001	7.2 %	3.7 %	3.7 %	4.7 %	<0.001
Atrial fibrillation/ flutter	17.1 %	12.3 %	12.5 %	13 %	<0.001	16.7 %	10.2 %	11.4 %	11.5 %	<0.001
Peripheral vascular disease	5.7 %	5.6 %	4.8 %	4 %	<0.001	2.5 %	3.5 %	2.5 %	2.3 %	0.02
Chronic lung disease	17.4 %	16 %	11 %	11 %	<0.001	9.7 %	9 %	7.3 %	7.4 %	<0.001
Chronic renal failure	13 %	21.9 %	16.6 %	15.3 %	<0.001	5.1 %	6.8 %	4 %	3.1 %	<0.001
Obesity	15.8 %	17.1 %	16.6 %	11.2 %	<0.001	5.7 %	5.1 %	6.7 %	4.7 %	0.008
Anaemia	16 %	24.6 %	20.1 %	20 %	<0.001	17.2 %	25 %	19.7 %	19.9 %	<0.001
Thrombocytopenia	4.6 %	5.3 %	5.3 %	6.1 %	<0.001	6.2 %	7.1 %	7.1 %	8 %	0.001
Coagulopathy	2 %	2.6 %	2.4 %	2.8 %	<0.001	4.5 %	8 %	4.4 %	3.7 %	<0.001
Dementia	4.5 %	5.5 %	4.4 %	4 %	<0.001	5.6 %	4.2 %	4.2 %	4.1 %	<0.001
Chronic Liver Disease	0.4 %	0.5 %	0.8 %	0.5 %	<0.001	0.4 %	0.5 %	0.6 %	1.2 %	<0.001
Homelessness	0.2 %	0.5 %	0.4 %	0.3 %	<0.001	0.1 %	1.3 %	0.6 %	0.2 %	<0.001
Solid malignancy	2.5 %	2.7 %	1.7 %	1.8 %	<0.001	3.4 %	4.6 %	2.3 %	2.7 %	<0.001
Hematologic Malignancies	0.9 %	0.9 %	0.7 %	0.6 %	<0.001	1.4 %	1.6 %	1 %	1.8 %	0.06
Metastatic cancer	1.2 %	1.4 %	0.9 %	0.9 %	<0.001	2 %	3.5 %	1.5 %	2.7 %	<0.001
In-Hospital procedures										
Coronary Angiography	84.5 %	77.5 %	84.1 %	84.9 %	<0.001	72.2 %	61.4 %	69.4 %	73.8 %	<0.001
PCI	73.5 %	63.1 %	71.7 %	71.8 %	<0.001	59.5 %	42.6 %	53.9 %	62.7 %	<0.001
CABG	5.1 %	3.6 %	5.7 %	6 %	<0.001	3.6 %	2.2 %	1.7 %	1.8 %	<0.001
Thrombolysis	0.5 %	0.6 %	0.6 %	0.7 %	<0.001	0.4 %	0.9 %	1 %	0.2 %	<0.001

SMuRF; standard cardiovascular modifiable risk factor, IQR; interquartile range, PCI; percutaneous coronary intervention, CABG; coronary artery bypass grafting surgery, MI; myocardial infarction.

NSTEMI[9]. Furthermore, to develop CAD in the absence of risk factors, host factors regarding susceptibility including inflammatory pathways may also be involved in heightened myocardial response to both MI adverse remodelling and arrhythmia burden[10].

All ethnic minority subgroups and White patients without any SMuRFs had worse outcomes than those with ≥ 1 SMuRFs. However, this was more apparent in ethnic minority patients, particularly Black patients with an increased likelihood of in-hospital mortality, MACCE, and major bleeding compared to White patients. Whilst unselected groups (in terms of risk factor profiles) of ethnic minorities have been shown to have worse outcomes for STEMI in contemporary US data [4,11], a significant portion has been attributed to their increased risk profiles with significantly higher rates of hypertension, hypercholesterolaemia, and diabetes compared to White patients[7,12]. Our analysis demonstrates that despite mitigation of these risk factors, the outcomes of ethnic minorities in STEMI are worse than White patients. This finding is even more surprising given their significantly younger age of presentation. Our analysis shows that Black patients without SMuRFs were significantly more likely to present with a cardiac arrest. There are likely to be prehospital factors that may affect how unwell the patients were on presentation.

Our analyses show that SMuRF-less patients were significantly less likely to undergo ICA and PCI than those with SMuRFs. This is likely multifactorial, with a part attributed to the increased perceived risk of patients with SMuRFs. It is also possible, that given the increased mortality and rates of cardiac arrest in this group, that they were less likely to receive invasive procedure, due to a rapid decline in their health. It is likely that they would have been considered for these procedures if they were to survive. Unfortunately, as we do not have the timing of the STEMI in relation to mortality, we are unable to fully explore this relationship, but it is important to mention. Given the worse outcomes in SMuRF-less patients, it is also possible that a proportion of the patients who are diagnosed as SMuRF-less may have been mis-classified. Whilst we do not have the exact data on prior hospitalisations for these patients, given their lack of perceived risk factors, it is possible that this could represent their first admission to hospital, thus, there may be instances of incomplete health records for these patients.

The overall poorer outcomes of SMuRF-less patients, particularly with respect to mortality compared to those with at least one modifiable risk factor, may reflect their overall poorer quality of care. This is

Table 5
In hospital outcomes of patients with and without SMuRF, by race.

	≥ 1 SMuRF					SMuRF-less				
	Whiten-300,190 (75.6 %)	Black n- 40,610 (10.2 %)	Hispanic n-30,135 (7.6 %)	Other n-25,935 (6.5 %)	P value	White n-26,855 (77.3 %)	Blackn-2,735 (7.8 %)	Hispanic n-2,595 (7.4 %)	Other n-2,560 (7.4 %)	P value
MACCE[1]	14.4 %	18.7 %	15.9 %	15.3 %	<0.001	27.9 %	37.7 %	28.7 %	31.6 %	<0.001
Mortality	9.8 %	12.2 %	10.8 %	10.7 %	<0.001	22.2 %	31.4 %	21.8 %	26.4 %	<0.001
Acute Ischemic CVA	2.1 %	4.3 %	2.6 %	2.2 %	<0.001	3.8 %	4.6 %	3.9 %	3.3 %	0.1
Cardiac Complications	3.7 %	4.1 %	3.9 %	3.8 %	0.005	5.6 %	5.7 %	6.9 %	5.7 %	0.05
Coronary artery dissection	1 %	1.1 %	1 %	0.8 %	0.006	2 %	1.6 %	2.7 %	1.8 %	0.03
Pericardial effusion (incl tamponade)	1.1 %	1.4 %	1.2 %	1.2 %	<0.001	1.9 %	2.9 %	2.7 %	2.7 %	<0.001
Tamponade	0.3 %	0.3 %	0.4 %	0.2 %	0.005	0.6 %	0.5 %	0.6 %	1.4 %	<0.001
Dressler's syndrome	0.4 %	0.5 %	0.5 %	0.4 %	0.71	0.4 %	<0.5 %*	<0.5 %*	<0.5 %	<0.001
Post MI angina	0.6 %	0.5 %	0.8 %	0.8 %	<0.001	0.4 %	<0.5 %*	<0.5 %*	0.8 %	0.003
Intracardiac Thrombus	0.4 %	0.6 %	0.3 %	0.6 %	<0.001	0.7 %	<0.5 %*	1 %	<0.5 %*	0.07
Mechanical complications[2]	0.3 %	0.1 %	0.2 %	0.2 %	<0.001	0.8 %	<0.5 %*	<0.5 %*	<0.5 %*	0.004
Vascular complications	0.2 %	0.1 %	0.2 %	0.2 %	0.001	0.2 %	0.7 %	<0.5 %*	<0.5 %*	<0.001
Major Bleeding	3.9 %	5.2 %	4.8 %	4.8 %	<0.001	6.2 %	10.4 %	7.1 %	8.8 %	<0.001
GI bleed	2.3 %	3 %	2.9 %	2.8 %	<0.001	3.8 %	5.7 %	3.3 %	5.5 %	<0.001
Procedural related bleeding	1 %	1 %	1 %	1.2 %	0.03	1.2 %	1.5 %	1.7 %	1 %	0.026
Retroperitoneal Bleed	0.2 %	0.3 %	0.3 %	0.2 %	<0.001	0.4 %	0.9 %	<0.5 %*	0.6 %	0.001
Intracranial Hemorrhage	0.5 %	1.1 %	0.8 %	0.8 %	<0.001	1.1 %	2.7 %	1.9 %	1.8 %	<0.001
Post procedural shock	0.4 %	0.5 %	0.4 %	0.7 %	<0.001	0.7 %	0.9 %	1 %	<0.5 %*	0.03

SMuRF; standard cardiovascular modifiable risk factor, MACCE; major adverse cardiovascular and cerebrovascular events, CVA; cerebrovascular accident.
*Exact number of patients not provided in order to avoid identifiable information.

Table 6
Adjusted Odds of SMuRF-less ethnic minority patients for in-hospital procedures and outcomes, compared to SMuRF-less White patients, by ethnicity.

	Black OR (95 % CI), p value	Hispanic OR (95 % CI), p value	Other OR (95 % CI), p value
Coronary Angiography	0.47 (0.43–0.52), p < 0.001	0.63 (0.57–0.69), p < 0.001	0.82 (0.74–0.9), p < 0.001
PCI	0.46 (0.42–0.5), p < 0.001	0.65 (0.6–0.71), p < 0.001	0.96 (0.88–1.06), p = 0.44
CABG	0.47 (0.36–0.62), p < 0.001	0.42 (0.3–0.57), p < 0.01	0.4 (0.29–0.55), p < 0.001
MACCE	1.63 (1.49–1.78), p < 0.001	1.29 (1.17–1.43), p < 0.001	1.24 (1.13–1.37), p < 0.001
Mortality **	1.9 (1.72–2.09), p < 0.001	1.31 (1.18–1.46), p < 0.001	1.4 (1.26–1.55), p < 0.001
Acute CVA**	1.07 (0.88–1.31), p = 0.49	1.13 (0.91–1.41), p = 0.26	0.88 (0.7–1.11), p = 0.28
Major Bleeding**	1.46 (1.27–1.69), p < 0.001	1.25 (1.06–1.48), p < 0.001	1.41 (1.2–1.64), p < 0.001

*Reference: White patients. Adjusted for Age, gender, weekend admission, hospital bed size, region and location/teaching status, cardiogenic shock, ventricular fibrillation, ventricular tachycardia, atrial fibrillation, heart failure, hypertension, dyslipidaemias, diabetes mellitus, valvular heart disease, smoking status, peripheral vascular disease, chronic lung disease, chronic liver disease, anaemia, thrombocytopenia, coagulopathies, malignancies, dementia.
** Reference: White patients. Adjusted for Age, gender, weekend admission, hospital bed size, region and location/teaching status, cardiogenic shock, ventricular fibrillation, ventricular tachycardia, atrial fibrillation, heart failure, hypertension, dyslipidaemias, diabetes mellitus, valvular heart disease, smoking status, peripheral vascular disease, chronic lung disease, chronic liver disease, anaemia, thrombocytopenia, coagulopathies, malignancies, dementia, coronary angiography, PCI, CABG.
OR – Odds Ratio, CI – confidence interval, SMuRF; standard cardiovascular modifiable risk factor, MACCE; major adverse cardiovascular and cerebrovascular events, CVA; cerebrovascular accident, PCI; percutaneous coronary intervention, CABG; coronary artery bypass grafting surgery.

evident, as this heterogeneous group received ICA, PCI, and CABG surgery less frequently than those with at least one SMuRF. An invasive strategy in the management of STEMI has been shown to significantly reduce mortality[13], and is the current *class 1a* recommendation of both European[14] and American[15] guidelines. It is important to note that the increased frequency of patients requiring mechanical ventilation in the SMuRF-less group may represent a cohort of much sicker patients.

Whilst in both the White and ethnic minority cohorts, the quality of care for SMuRF-less patients with respect to invasive management was inferior in comparison to those who had more than one SMuRF, the frequency of being treated invasively was significantly lower and varied according to the ethnic minority subgroup. Black and Hispanic patients were significantly less likely to receive ICA, PCI, or CABG surgery compared to White patients. In part, this may contribute to their worse mortality outcomes. However, there is likely a complex interplay of cultural practices and socioeconomic factors, and phenotypical differences that account for their differences in care and outcomes. Aside from differences in risk factor profiles, Black patients presenting with STEMI are less likely to have health insurance, poorer education access, and lower incomes in the US[16]. Lower socioeconomic status may be linked to reduced compliance with secondary prevention therapies due to the cost of medication and reduced access to healthcare[17]. Furthermore, there may be implicit physician bias which has been previously indicated as a potential reason for poorer quality of care in certain ethnic minority groups[18].

Our analysis has several clinical implications for practice. We add to the growing body of evidence that a significant proportion of CAD is not attributed to the known SMuRFs. This finding is particularly important, as a paradigm shift is required where CAD is not solely viewed a self-induced problem. Population-based data such as the INTERHEART study has had an important societal effect and helped shape health policy. However, misunderstanding of their results may have halted efforts to unravel new mechanisms of disease. Whilst the study demonstrated that nine conventional risk factors explained the vast majority of premature MI, the findings are commonly misunderstood as equating only a small minority of disease burden being attributed to other cardiovascular risk factors[19–21].

Furthermore, our analysis highlights that there are disparities of care which is reflected in the quality of care and outcomes of ethnic minority patients without SMuRFs. Whilst it is disappointing that the quality of care for ethnic minority patients without SMuRFs is inferior to patients who are White, it is surprising that their outcomes, particularly mortality, are significantly worse given the mitigation of known risk factors, which are significantly higher in the various ethnic minority populations. This highlights the importance of not only addressing primary and secondary prevention measures for AMI but looking further for

Table 7
Adjusted OR of SMuRF-less patients for In-Hospital procedures, by race.

	White OR (95 %CI), p value	Black OR (95 %CI), p value	Hispanic OR (95 %CI), p value	Other OR (95 %CI), p value
Coronary Angiography*	0.75 (0.72–0.78), p < 0.001	0.62 (0.56–0.7), p < 0.001	0.56 (0.49–0.63), p < 0.001	0.7 (0.62–0.8), p < 0.001
PCI*	0.7 (0.68–0.73), p < 0.001	0.59 (0.53–0.65), p < 0.001	0.48 (0.43–0.53), p < 0.001	0.68 (0.61–0.76), p < 0.001
CABG*	1.3 (1.2–1.41), p < 0.001	1.22 (0.88–1.68), p = 0.23	0.9 (0.63–1.28), p = 0.54	0.43 (0.3–0.6), p < 0.001
MACCE**	1.38 (1.32–1.44), p < 0.001	1.17 (1.04–1.32), p < 0.001	1.44 (1.26–1.65), p < 0.001	1.69 (1.47–1.95), p < 0.001
Mortality **	1.45 (1.38–1.53), p < 0.001	1.44 (1.25–1.65), p < 0.001	1.52 (1.29–1.59), p < 0.001	1.86 (1.58–2.2), p < 0.001
Acute CVA**	1.49 (1.36–1.64), p < 0.001	0.63 (0.5–0.8), p < 0.001	1.23 (0.92–1.65), p = 0.17	1.17 (0.86–1.6), p = 0.31
Major Bleeding**	1 (0.94–1.08), p = 0.93	1.16 (0.97–1.4), p < 0.001	0.9 (0.73–1.12), p = 0.35	0.9 (0.72–1.11), p = 0.33

*Reference: Patients with ≥ 1 SMuRFs. Adjusted for Age, gender, weekend admission, hospital bed size, region and location/teaching status, cardiogenic shock, ventricular fibrillation, ventricular tachycardia, atrial fibrillation, heart failure, hypertension, dyslipidaemias, diabetes mellitus, valvular heart disease, smoking status, peripheral vascular disease, chronic lung disease, chronic liver disease, anaemia, thrombocytopenia, coagulopathies, malignancies, dementia.
** Reference: Patients with ≥ 1 SMuRFs. Adjusted for Age, gender, weekend admission, hospital bed size, region and location/teaching status, cardiogenic shock, ventricular fibrillation, ventricular tachycardia, atrial fibrillation, heart failure, hypertension, dyslipidaemias, diabetes mellitus, valvular heart disease, smoking status, peripheral vascular disease, chronic lung disease, chronic liver disease, anaemia, thrombocytopenia, coagulopathies, malignancies, dementia, coronary angiography, PCI, CABG.
OR – Odds Ratio, CI – confidence interval, SMuRF; standard cardiovascular modifiable risk factor, MACCE; major adverse cardiovascular and cerebrovascular events, CVA; cerebrovascular accident, PCI; percutaneous coronary intervention, CABG; coronary artery bypass grafting surgery.

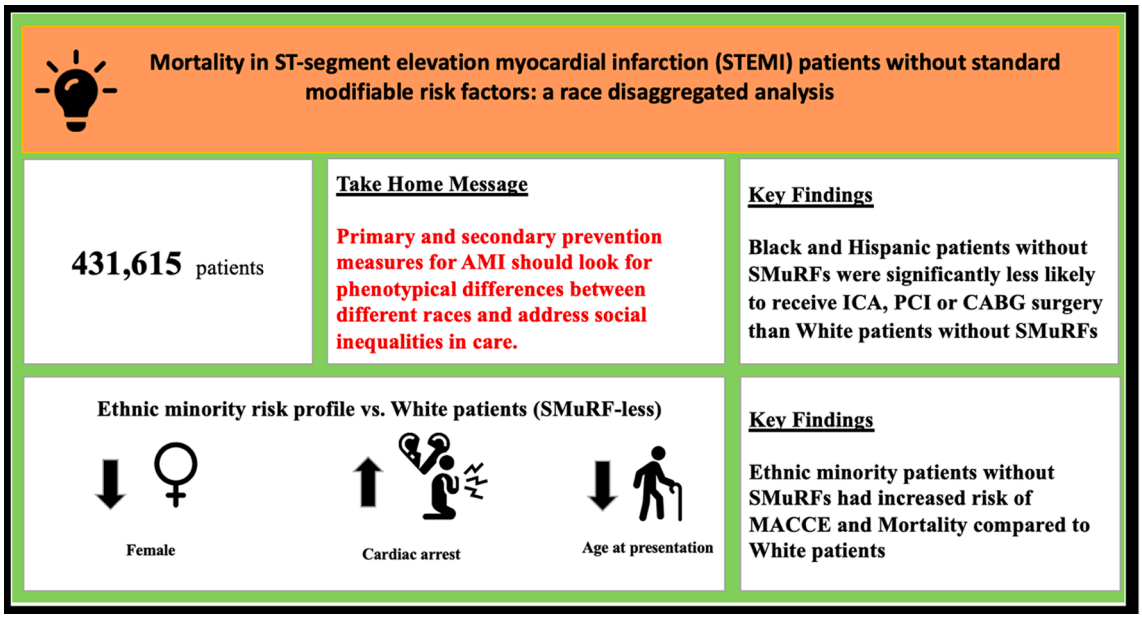

Fig. 2. Central Illustration, SMuRF; standard cardiovascular modifiable risk factor, MACCE; major adverse cardiovascular and cerebrovascular events, CVA; cerebrovascular accident, PCI; percutaneous coronary intervention, CABG; coronary artery bypass grafting surgery.

other differences between different races and the importance of addressing social inequalities in care.

There are several strengths of this investigation. Our analysis represents the largest study to date from a healthcare system that looks at the characteristics and outcomes of SMuRF-less patients, and the first that disaggregates the analysis according to race. The NIS database gives insight into the "real world" in-hospital clinical outcomes on a large and unselected cohort of patients with AMI, including those that are high risk and have multiple comorbid illnesses, such that they are either not included or underrepresented in clinical trials. Due to the size of the database, there is sufficient power to detect differences in adverse clinical outcomes between the two cohorts of interest.

There are several important limitations to our present study. Despite the NIS using ICD-9 and 10 codes and being a validated and exhaustive dataset for the purposes of cardiovascular research[22,23], it is an administrative dataset, and coding error may be a source of bias. The identification of STEMI, hypertension, hypercholesterolaemia, diabetes mellitus, smoking status, race as well as other comorbidities and procedural data was based on the use of administrative codes. Second, the NIS dataset only records in-hospital outcomes, and therefore longer-term follow-up of mortality or other adverse outcomes are missing from our analysis. Third, the database does not include pharmacotherapy. Thus, we cannot determine if there was a significant disparity in care between the two groups regarding pharmacotherapy or to see if the use of pharmacotherapy altered clinical outcomes for patients without SMuRFs. Fourth, the database does not capture markers of inflammation, biomarkers, LDL-cholesterol levels, or lipoprotein (a)[24]. Fifth, a proportion of patients without SMuRFs may have a subclinical disease or may have risk factors that were not previously diagnosed. Furthermore, like other administrative datasets, it does not capture the ethnicity of the physician or other allied health professionals, which may impact management.

5. Conclusion:

Our study demonstrated that from 2015 to 2018, almost one in ten

patients in the US who presented with STEMI had no standard cardiovascular modifiable risk factors. Patients without SMuRFs had increased in-hospital mortality and MACCE compared to those with at least one SMuRF. They were less likely to be treated invasively and had a lower frequency of ICA, PCI, or CABG surgery. Our race-disaggregated analysis showed outcomes of in-hospital mortality, MACCE, and major bleeding were significantly worse for ethnic minorities (particularly Black patients) with no SMuRFs compared to White patients. The quality of care was inferior, with a reduction in the use of ICA and PCI. More substantial work is needed to raise the awareness of patients with no SMuRFs presenting with STEMI. Future work should aim to look at differences in aetiology and pathophysiology between SMuRF-less patients and those presenting with known risk factors, particularly with respect to race.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2022.101135.

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