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Management and outcomes of patients admitted with type 2 myocardial infarction with and without standard modifiable risk factors☆

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ABSTRACT

Background: Whilst it is known patients without standard modifiable cardiovascular risk factors (SMuRF; hypertension, diabetes, hypercholesterolaemia, smoking) have worse outcomes in Type 1 acute myocardial infarction (AMI), the relationship between type 2 AMI (T2AMI) and outcomes in patients with and without SMuRF is unknown. This study aimed to determine the prevalence, characteristics and clinical outcomes of patients hospitalised with T2AMI based on the presence of SMuRF.

Methods: Using the National Inpatient Sample, all hospitalizations with a primary discharge diagnosis of T2AMI were stratified according to SMuRF status (SMuRF and SMURF-less). Primary outcome was all-cause mortality while secondary outcomes were major adverse cardiovascular and cerebrovascular events (MACCE), major bleeding and ischemic stroke. Multivariable logistic regression was used to determine adjusted odds ratios (aOR) with 95% confidence intervals (95% CI).

Results: Among 17,595 included hospitalizations, 1345 (7.6%) were SMuRF-less and 16,250 (92.4%) were SMuRF. On adjusted analysis, SMuRF-less patients had increased odds of all-cause mortality (aOR 2.43, 95% CI 1.83 to 3.23), MACCE (aOR 2.32, 95% CI 1.79 to 2.90) and ischaemic stroke (aOR 2.57, 95% CI 1.56 to 4.24) compared to their SMuRF counterparts. Secondary diagnoses among both cohorts were similar, with respiratory disorders most prevalent followed by cardiovascular and renal disorders.

Conclusions: T2AMI in the absence of SMuRF was associated with worse in-hospital outcomes compared to SMuRF-less patients. There was no SMuRF-based difference in the secondary diagnoses with the most common being respiratory, cardiovascular, and renal disorders. Further studies are warranted to improve overall care and outcomes of SMuRF-less patients.

1. Introduction

Prevention of cardiovascular disease is an important public health goal targeted towards treating the standard modifiable cardiovascular risk factors (termed SMuRF) of smoking, dyslipidemia, diabetes, and hypertension (HTN) [1]. However, up to 25% of patients admitted with ST segment elevation myocardial infarction (STEMI) have no SMuRF (termed SMuRF -less) [2–5]. Studies have demonstrated that SMuRF-less patients admitted for STEMI have a 47% increased risk of all-cause mortality compared with patients with at least one modifiable risk factor [3]. In contrast, in the setting of non-STEMI (NSTEMI), SMuRF-less patients were less likely to experience in-hospital mortality and major

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adverse cardiovascular events compared to patients with SMuRF [2,5]. SMuRF-less patients are more likely to be older, female and white compared to SMuRF patients and are underrepresented in clinical trial populations [2,3,6–8].

Type 2 acute myocardial infarction (T2AMI) is caused by a supply-demand mismatch of blood flow to the myocardium [6]. The reported incidence of T2AMI varies between 8.5% to 43% of AMI hospitalizations and is associated with a poorer prognosis compared to type 1 AMI (T1AMI), with higher rates of major bleeding and mortality [9,10]. The underlying mechanisms of T2AMI are heterogeneous with a diverse patient risk profile leading to differences in the management and outcomes of these patients [11]. However, there are no current studies investigating the outcomes of patients presenting with T2AMI based on SMuRF status.

This study therefore aimed to investigate the prevalence, characteristics, and clinical outcomes of patients with and without SMuRF admitted with T2AMI using a national cohort of patients. Furthermore, we aimed to investigate the utilization of invasive management and the main secondary diagnoses of patients with and without SMuRF admitted for T2AMI.

2. Methods

The National Inpatient Sample (NIS) is the largest publicly available database of US hospitalisations developed for the Healthcare Cost and Utilization Project (HCUP) and is sponsored by the Agency for Healthcare Research and Quality (AHRQ) [12]. The dataset contains anonymised data on diagnoses and procedures from over 7 million hospitalisations annually, representing a 20% stratified sample of all discharges form US community hospitals, excluding rehabilitation and long-term acute care hospitals, with the sample representing >95% of the US population [12].

All adult hospitalizations between 2017 and 2018 with a principal discharge diagnosis of T2AMI were identified using the International Classification of Diseases 10th revision (ICD-10) codes. Cases were stratified by their risk factors into SMuRF and SMuRF-less groups. SMuRF status was defined by the presence of one or more SMuRF, including diabetes mellitus, dyslipidaemia, hypertension, or a current smoking history [13]. The ICD-10 codes were used to extract data on patient characteristics, co-morbidities, management strategies and hospital outcomes (Supplementary Table S1).

Cases were excluded due to missing data for the following variables: age, sex, weekend admission, elective admission, in-hospital mortality, primary expected payer, hospital bed size, hospital location and length of stay. These cases accounted for no >0.8% of the original dataset (Supplementary Fig. S1). Analyses were weighted using discharge weights as recommended by HCUP. To improve the quality of this observational study, *Strengthening The Reporting of OBservational Studies in Epidemiology* (STROBE) checklist was included in Appendix A.

The primary outcome of this study was in-hospital all-cause mortality. Secondary outcomes included other adverse in-hospital outcomes such as major acute cardiovascular and cerebrovascular events (MACCE), major bleeding, acute ischaemic stroke, and acute haemorrhagic stroke. Furthermore, we aimed to investigate whether SMuRF status influenced the receipt of invasive management for AMI, coronary angiography (CA) and percutaneous coronary intervention (PCI). Finally, the study aimed to investigate SMuRF-based differences in the secondary diagnoses.

Continuous variables such as age, length of hospital stay and total charges were summarised using median and interquartile range (IQR). Categorical variables were compared using the Chi-squared (X^2) test and summarised as percentages (%). Multivariable logistic regression was performed to determine the adjusted odds ratio (aOR) for invasive management and adverse outcomes. Regression model was adjusted for the following variables due to its relevance for the outcomes: bed size of hospital, region of hospital, teaching status of hospital, age, sex, race, weekend admission, elective admission, primary expected payer, median household income, cardiogenic shock, thrombocytopenia, previous cerebrovascular incident (CVI; stroke or transient ischemic attack), anemia, chronic lung disease, atrial fibrillation (AF), coagulopathies, liver disease, solid tumors, hematological malignancy, metastatic disease, peripheral vascular disease (PVD), valvular heart disease, dementia. Results were presented as adjusted odds ratios (aOR) with 95% confidence intervals (CI). Results were determined significant at the level of $p < 0.05$. All statistical analyses were performed using SPSS version 27 (IBM Corp, Armonk, NY) [14].

3. Results

3.1. Baseline characteristics

A total of 17,595 T2AMI admissions were identified, of which 16,250 (92.4%) patients were SMuRF and 1345 (7.6%) were SMuRF-less (Supplementary Fig. S1). SMuRF-less patients were on average 6 years younger (median age 65 vs. 71 years, $p < 0.001$), more likely to be female (55.8% vs. 53.1%, $p = 0.032$) and white (78.4% vs. 68.6%, $p < 0.001$). The SMuRF-less group had a lower prevalence of comorbidities such as atrial fibrillation (26.0% vs. 30.9%, $p < 0.001$), prior stroke (3.7% vs. 8.7%, $p < 0.001$), anemia (21.2% vs. 26.4%, $p < 0.001$), PVD (0.4% vs. 5.8%, $p < 0.001$) and chronic renal failure (12.6% vs. 32.0%, $p < 0.001$) (Table 1).

3.2. Secondary diagnoses

When looking at the secondary diagnoses among study groups, respiratory disorders were the most frequent secondary diagnosis in both SMuRF-less and SMuRF patients (39.8% and 37.0%, respectively), followed by cardiovascular disorders (22.7% and 16.1%, respectively) and acute renal failure/urinary tract disorders (7.1% and 10.5%, respectively) (Supplementary Table 2–3, Fig. 1). The three most common secondary diagnoses in SMuRF patients were acute respiratory failure with hypoxia, acute on chronic diastolic heart failure and acute renal failure (4.92%, 4.65% and 4.52% respectively) (Supplementary Table 2). The three most common secondary diagnoses in SMuRF-less patients were pneumonia, acute respiratory failure with hypoxia, and supraventricular tachycardia (8.18%, 5.58% and 4.83% respectively) (Supplementary Table 3).

3.3. Invasive management

SMuRF-less patients had significantly lower rates of CA and PCI procedures compared to the SMuRF group (33.5% vs. 34.4%, $p < 0.001$, and 1.9% vs. 5.2%, respectively) (Supplementary Table 4 and Supplementary Fig. 2). When adjusting for baseline characteristics, SMuRF-less patients were significantly less likely to be managed invasively with CA or PCI (aOR 0.75, 95% CI 0.66 to 0.86 and aOR 0.35, 95% CI 0.23 to 0.53, respectively) (Table 2).

3.4. Clinical outcomes

SMuRF-less patients had higher crude rates of in-hospital all-cause mortality (5.9% vs. 3.0%, $p < 0.001$), MACCE (7.1% vs. 3.8%, $p < 0.001$), major bleeding (4.5% vs. 3.8%, $p = 0.046$) and ischaemic stroke (1.9% vs. 0.8%, $p < 0.001$) (Supplementary Table 4 and Supplementary Fig. 3). When adjusted for differences in baseline characteristics, SMuRF-less patients had increased odds of all-cause mortality (aOR 2.43, 95% CI 1.83 to 3.23), MACCE (aOR 2.32, 95% CI 1.79 to 2.90) and ischaemic stroke (aOR 2.57, 95% CI 1.56 to 4.24) compared to their SMuRF counterparts, while there was no difference in major bleeding ($p = 0.095$) (Table 2 and Fig. 2).

Table 1
Baseline patient characteristics based of Type 2 AMI according SMuRF status.

Characteristics	SMuRF (92.4%)	SMuRF-less (7.6%)	Overall T2AMI Cohort	*P*-value
Number of hospitalizations	16,250	1345	17,595	
Age (years), median (IQR)	71 (60, 82)	65 (53, 78)	70 (59, 81)	<0.001
Female sex, %	53.1	55.8	53.3	0.032
Race, %				<0.001
White	68.6	78.4	69.4	
Black	20.6	11.2	19.8	
Hispanic	6.4	5.6	6.4	
Other	4.4	4.8	4.4	
Weekend admission, %	26.3	31.2	26.7	<0.001
Primary expected payer, %				<0.001
Medicare	67.0	53.2	66.0	
Medicaid	11.2	10.0	11.1	
Private Insurance	16.4	28.3	17.3	
Self-pay	3.0	4.5	3.1	
No charge	0.4	1.1	0.5	
Other	1.9	3.0	2.0	
Median Household Income (percentile), %				<0.001
0-25th	35.5	26.0	34.8	
26th–50th	28.6	27.1	28.5	
51st-75th	20.4	21.6	20.5	
76th–100th	15.5	25.3	16.2	
Cardiogenic shock, %	2.3	2.6	2.3	0.271
Cardiac arrest, %	1.5	3.0	1.6	<0.001
Ventricular tachycardia, %	4.1	5.2	4.1	0.029
Ventricular fibrillation, %	0.9	1.1	0.9	0.359
Comorbidities, %				
Atrial fibrillation	30.9	26.0	30.5	<0.001
Thrombocytopenia	5.8	5.2	5.8	0.183
Previous CVI	8.7	3.7	8.3	<0.001
Anemias	26.4	21.2	26.0	<0.001
Heart failure	52.2	36.4	51.0	<0.001
Valvular disease	19.0	13.0	18.5	<0.001
Peripheral vascular disorders	5.8	0.4	5.3	<0.001
Chronic pulmonary disease	28.7	22.3	28.2	<0.001
Coagulopathy	7.3	5.6	7.1	0.010
Dementia	10.5	6.3	10.1	<0.001
Liver disease	4.3	7.4	4.5	<0.001
Chronic renal failure	32.0	12.6	32.0	<0.001
Metastatic cancer	1.9	3.7	2.0	<0.001
Bed size of hospital, %				0.305
Small	20.4	21.6	20.5	
Medium	29.1	30.1	29.2	
Large	50.5	48.3	50.3	
Hospital Region, %				<0.001
Northeast	27.2	34.6	27.8	
Midwest	31.5	27.9	31.3	
South	38.2	35.3	38.0	
West	3.0	2.2	3.0	
Location/teaching status of hospital, %				0.004
Rural	10.5	13.4	10.7	
Urban non-teaching	18.5	17.8	18.5	
Urban teaching	71.0	68.8	70.8	

Abbreviations: AMI – Acute Myocardial Infarction; CABG – Coronary Artery Bypass Graft; CVI – Cerebrovascular Incidents; IHD – Ischemic Heart Disease; IQR – Interquartile Range; PCI – Percutaneous Coronary Intervention; SMuRF – Standard modifiable cardiovascular risk factor; STEMI – ST-elevation Myocardial Infarction; T2AMI – Type 2 Acute Myocardial Infarction.

3.5. Analysis including obesity within SMuRF

Similar results were observed with obesity included within the SMuRF variable (Supplementary Table 5 and 6). SMuRF-less patients were less likely to receive invasive management with CA (aOR 0.73, 95% CI 0.63 to 0.84) and PCI (aOR 0.39, 95% CI 0.26 to 0.59) and more likely to experience all-cause mortality (aOR 2.56, 95% CI 1.91 to 3.43),

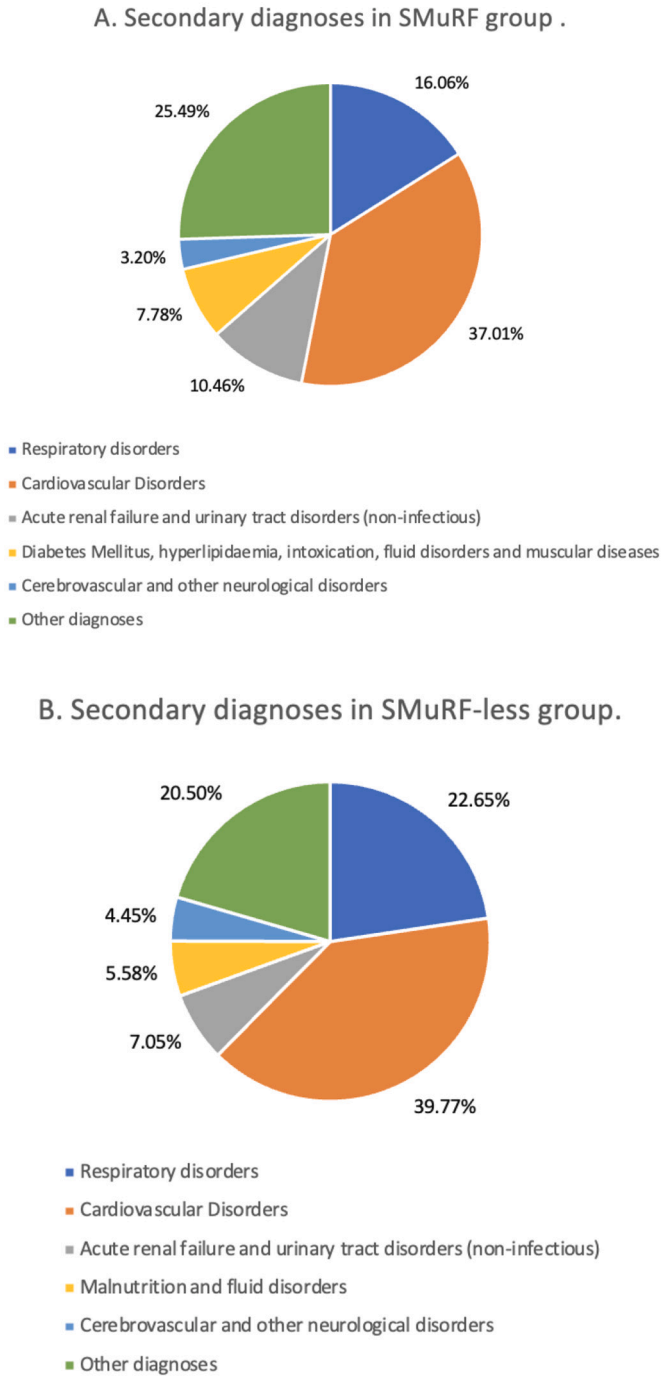

Fig. 1. Secondary diagnoses of in SMuRF and SMuRF-less groups: A. Secondary diagnoses in SMuRF group; B. Secondary diagnoses in SMuRF-less group. Abbreviations: SMuRF - Standard modifiable cardiovascular risk factor.

MACCE (aOR 2.46, 95% CI 1.90 to 3.20) and ischaemic stroke (aOR 2.89, 95% CI 1.75 to 4.77) (Supplementary Table 6).

4. Discussion

The present study is the first to examine the prevalence, characteristics, and clinical outcomes of over 17,000 T2AMI patients, stratified by their SMuRF status. There have been no prior studies investigating the effect of SMuRF status on the characteristics and outcomes of T2AMI patients. We report several important findings. Firstly, the proportion of SMuRF-less patients presenting with T2AMI (7.6%) is lower than has

Table 2
Adjusted odds ratios (aOR) of in-hospital invasive management and clinical outcomes of Type 2 AMI in the SMuRF-less group*.

Variables	SMuRF-less	
	aOR [95% CI]	*P*-value
Invasive management:		
Coronary angiography	0.75 [0.66–0.86]	<0.001
PCI	0.35 [0.23–0.53]	0.349
CABG	0.48 [0.27–0.87]	0.015
Clinical outcomes:		
All-cause mortality	2.43 [1.83–3.23]	<0.001
MACCE	2.32 [1.79–2.90]	<0.001
Major bleeding	1.28 [0.96–1.72]	0.095
Ischemic stroke	2.57 [1.56–4.24]	<0.001

Multivariable logistic regression model adjusted for: age, sex, race, weekend admission, elective admission, primary expected payer, median household income, hospital bed size, region and teaching status, cardiogenic shock, thrombocytopenia, previous cerebrovascular incident (CVI; stroke or transient ischemic attack), anemia, chronic lung disease, atrial fibrillation (AF), coagulopathies, liver disease, solid tumors, hematological malignancy, metastatic disease, peripheral vascular disease (PVD), valvular heart disease, dementia.
Abbreviations: aOR – adjusted odds ratios; MACCE – major adverse cardiovascular and cerebrovascular events (composite of mortality, acute stroke/transient ischemic attack and reinfarction); NSTEMI – non-ST-elevation myocardial infarction; PCI – Percutaneous coronary intervention; SMuRF – Standard modifiable cardiovascular risk factor; STEMI – ST-elevation myocardial infarction.
* Reference group is group with SMuRF.

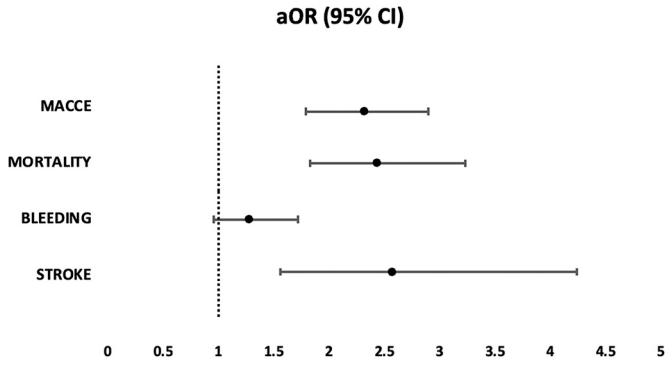

Fig. 2. Adjusted odds ratios (aOR) of in-hospital clinical outcomes of SMuRF-less patients with Type 2 AMI.
* Reference group is group with SMuRF.
Multivariable logistic regression model adjusted for: age, sex, race, weekend admission, elective admission, primary expected payer, median household income, hospital bed size, region and teaching status, cardiogenic shock, thrombocytopenia, previous cerebrovascular incident (CVI; stroke or transient ischemic attack), anemia, chronic lung disease, atrial fibrillation (AF), coagulopathies, liver disease, solid tumors, hematological malignancy, metastatic disease, peripheral vascular disease (PVD), valvular heart disease, dementia.
Abbreviations: aOR – adjusted odds ratios; MACCE – major adverse cardiovascular and cerebrovascular events (composite of mortality, acute stroke/transient ischemic attack and reinfarction); SMuRF – Standard modifiable cardiovascular risk factor.

been reported in T1AMI studies (14–27% for STEMI and 3.7% to 23% for NSTEMI) [2,3,5,15,16]. Secondly, SMuRF-less patients were more likely to be younger, white, and female with fewer comorbidities than SMuRF patients. Thirdly, there were no major differences in the main secondary diagnostic groups of the patients with T2AMI by SMuRF status, even though there were some differences within each diagnostic category. Fourthly, SMuRF-less patients had worse in-hospital clinical outcomes including all-cause mortality, MACCE and ischaemic stroke. Finally, whilst invasive management is not routinely indicated for T2AMI, there were important SMuRF-based differences in the utilization of invasive management, suggesting the importance of conventional risk factors during physician's decision-making about CA and PCI.

Numerous studies have reported the prevalence of SMuRF-less first time STEMI patients to be around 15% [17]. Figtree et al. identified 14.9% SMuRF-less patients in the SWEDEHEART STEMI sub-cohort, while another study by the same group using the Australian Global Registry of Acute Coronary Events (GRACE) and the Cooperative National Registry of Acute Coronary Syndrome Care (CONCORDANCE) registries identified a SMuRF-less prevalence in STEMI patients of 19% [3,5]. A study of SMuRF in a NSTEMI cohort derived using the United Kingdom Myocardial Infarction National Audit Project (MINAP) found as much as 23% of patients were SMuRF-less, whereas a study centred around an Asian population found only 8.6% of patients were SMuRF-less [2,18]. However, none of these studies focussed on a T2AMI cohort. Interestingly, while these studies were conducted on T1AMI population, our analysis identified a much lower prevalence of SMuRF-less patients within a T2AMI cohort. The lower prevalence of SMuRF-less patients may be explained by the aetiology of T2AMI. T2AMI is defined as an acute myocardial injury due to supply-demand imbalance in the absence of acute atherosclerotic coronary lesion [19]. This is usually due to another secondary disease process causing this imbalance such as respiratory disorders and renal disorders and often the presence of established coronary artery disease- either epicardial or microvascular- that may compromise myocardial perfusion [11,19]. SMuRF also contribute as risk factors for disorders causing T2AMI, and therefore, the lower prevalence of SMuRF in our cohort may be mediated by this [5].

In our study of T2AMI patients, we found that SMuRF-less patients were more likely to be female, white and younger with generally less comorbidities. Ethnic minority groups have previously been shown to have increased rates of diabetes mellitus, hypertension and hypercholesterolaemia when presenting with AMI, thus explaining the lower prevalence of non-white patients in the SMuRF-less cohort [2,15,20], and vice versa, the lower rates SMuRF individuals from many Asian backgrounds [16]. The majority of studies on T1AMI cohort have shown SMuRF-less patients are either a similar age or older than SMuRF patients [2,3,5,16,20]. Consistent to this study, an analysis of Asian T1AMI cohort showed SMuRF-less patients were younger compared to their counterparts [18]. The study proposed genetic risk could be a factor resulting in earlier presentation of AMI in SMuRF-less patients [18].

While previous studies on T1AMI patients have shown that SMuRF status is an important consideration, SMuRF-less patients are mostly underrepresented in trial populations [2,5,7]. The reported outcomes of SMuRF-less patients are conflicting. A study of 3081 STEMI patients by Vernon et al. found SMuRF-less patients had a higher mortality compared to SMuRF patients, in agreement with other studies of STEMI patients [3,5,16,18]. Similarly, our analysis shows SMuRF-less patients presenting with T2AMI had increased risk of mortality, MACCE and stroke. The causes are poorly understood and are likely multifactorial. The SMuRF-less cohort likely include those with missed standard modifiable risk factors (which may have poor prognostic impact in a causal manner). They may include patients with atypical risk factors such as liver disease or cancer associated with worse prognosis, as shown in the present study and several others [3,9,21–23], but observed not to be an explanation in the SWEDEHEART STEMI cohort. The third category of SMuRF-less AMI individuals particularly relevant to those with demonstrated atherosclerosis and vascular dysfunction, are those with true heightened susceptibility to these processes in the absence of risk factors. This may reflect augmentation of inflammatory or oxidative pathways, or, perhaps, completely novel mechanisms that we are yet to unravel. It is biologically feasible that such heightened responses may also be relevant to myocardial responses and be mechanistically involved in increased susceptibility to arrhythmia [8]. The key mechanism of heightened mortality in the STEMI population from SWEDEHEART in the first 30 days appeared to be arrhythmia [3]. And a consistent signal, including in this analysis, is the 2 fold higher rates of cardiac arrest. In this T2AMI population, VF and primary cardiac

arrhythmia may be a smaller proportion of the cardiac arrests, particularly given the contribution of respiratory causes.

Several conditions are associated with T2AMI, however there is very little data specifying their prevalence. In our analysis we found SMuRF and SMuRF-less patients had similar secondary diagnoses, with respiratory disorders most prevalent, followed by cardiovascular and renal disorders which was in consistent with other studies [9,22,23]. This is important as the difference in the T2AMI outcomes cannot be associated with the underlying secondary diagnosis, but with the non-accountable characteristics of the population with a common endpoint of myocardial injury. Higher mortality rates in SMuRF-less patients compared to SMuRF patients could also be due to pharmacological management. The inherent higher rates of modifiable cardiovascular risk factors (by definition of the group) as well as atrial fibrillation in SMuRF patients increases their likelihood of being on preventative treatment such as angiotensin converting enzyme inhibitors, anti-thrombotics, beta blockers and statin therapy. This may be a contributing factor to the lower rates of mortality seen in the setting of T2AMI compared to their SMuRF-less counterparts [6].

There are several important clinical implications of this study. We reaffirm that SMuRF-less patients form a significant population of T2AMI hospitalizations. Current attitudes for cardiovascular prevention focus mostly on SMuRF patients, viewing cardiovascular risk as self-induced. Our findings suggest a change in this perspective when looking at the T2AMI patients, which is in line to previous reports on T1AMI population. The current study highlights the need to improve patient stratification, with overall risk profile recognition, and to raise awareness of the higher early mortality risk of SMuRF-less patients. Finally, this study generates new hypotheses warranting further investigation of the mechanisms behind worse in-hospital outcomes in the SMuRF-less T2AMI population.

The limitations of this study include several inherent to the use of the NIS database. Firstly, coded data for the NIS could be subject to selection bias due to inaccuracies with coding and missing data. Nevertheless, the low rates of revascularisation in this cohort would suggest that that T2AMI patient cohort is unlikely to contain significant numbers of patients with T1AMI. Secondly, detailed clinical information that could be used to better risk stratify the patient population such as left ventricular function, renal function, infarct size, timing and completeness of revascularization, postprocedural Thrombolysis in Myocardial Infarction (TIMI) flow, anti-thrombotic and secondary prevention regimes could not be investigated due to their lack of availability with the NIS. Thirdly, as this is an observational study, residual confounding bias could not be fully eliminated despite the broad scope of conditions covered by the NIS and adjusted for. Finally, study design allows only evaluation of associations and doesn't implicate any cause-effect findings.

5. Conclusions

In conclusion, this analysis reveals that SMuRF-less patients represent a minority of those admitted for T2AMI but are more likely to suffer adverse in-hospital outcomes and are less likely to be managed invasively. Although there are important differences in baseline characteristics, there was no SMuRF-based difference in secondary diagnoses. These findings warrant further studies to improve overall care and outcomes of SMuRF-less patients.

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CRediT authorship contribution statement

Balamrit Singh Sokhal: Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Visualization. **Andrija Matetić:** Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Visualization, Supervision. **Timir K. Paul:** Writing – review & editing. **Poonam Velagapudi:** Writing – review & editing. **Ekaterini Lambrinou:** Writing – review & editing. **Gemma A. Figtree:** Writing – review & editing. **Muhammad Rashid:** Writing – review & editing. **Saadiq Moledina:** Writing – review & editing. **Vassilios S. Vassiliou:** Writing – review & editing. **Christian Mallen:** Writing – review & editing. **Mamas A. Mamas:** Conceptualization, Writing – original draft, Writing – review & editing, Supervision, Project administration.

Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2022.09.037.

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