Effect of Chronic Hematologic Malignancies on In-Hospital Outcomes of Patients With ST-Segment Elevation Myocardial Infarction

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In view of hemorrhagic and prothrombotic tendencies, ST-segment elevation myocardial infarction (STEMI) patients with chronic hematologic malignancies (CHM) are felt to be at a higher risk and hence denied standard reperfusion strategies. In-hospital outcomes of CHM patients presenting with STEMI are unclear. The Nationwide Inpatient Sample data files from 2003 to 2014 were used to extract adult patients who presented with a primary diagnosis of STEMI. Patients who had a diagnosis of CHM defined as chronic myelogenous leukemia, chronic lymphocytic leukemia, essential thrombocythemia, polycythemia vera, chronic monocytic leukemia, and multiple myeloma were identified. The primary study outcome measure was in-hospital mortality. Inverse probability weighting-adjusted binary logistic regression was performed to identify independent predictors of in-hospital mortality. Of 2,715,807 STEMI patients included in the final analyses, 11,974 (0.4%) patients had a diagnosis of CHM. Patients with CHM were significantly older, had a higher prevalence of co-morbidities, and had a significantly higher unadjusted in-hospital mortality (14.9% vs 9.0%; p <0.001). After adjusting for co-morbidities, CHM did not independently predict a higher in-hospital mortality (odds ratio = 1.02, 95% confidence interval = 0.96 to 1.09; p = 0.461). In patients with CHM who presented with STEMI, percutaneous coronary intervention was found to be associated with a significant reduction in in-hospital mortality (odds ratio = 0.22, 95% confidence interval = 0.18 to 0.27; p <0.001) (c-statistic = 0.81). In conclusion, CHM patients presenting with STEMI should be treated with similar treatment strategies as those without CHM, including revascularization if indicated, as there appears to be a sizable outcome advantage with this approach. **(Am J Cardiol 2019;124:349−354)**

Improvements in oncologic therapies as well as other factors have led to an unprecedented increase in cancer survivors, including those with chronic hematologic malignancies (CHM), with further increase expected in the future.[1−3] Historically, oncologic patients are felt to have limited prognosis, and hence have been felt unsuitable for aggressive cardiovascular therapies. Increased prevalence of risk factors in these patients, as well as cardiotoxic effect of cancer treatment is expected to increase the burden of patients with malignancy and cardiovascular disease.[4] With the improving prognosis from an oncologic standpoint, the approach to outcome changing cardiovascular disease in these patients' subset needs a paradigm shift. Patients with CHM are challenging to manage when they develop ST-segment elevation myocardial infarction (STEMI) in view of associated prothrombotic as well as hemorrhagic tendencies.[5,6] With improvements in stent technology, evidence supporting the safety of shorter duration of dual antiplatelet therapy,[7] percutaneous coronary intervention (PCI) as a therapeutic modality has become a possibility in these complex patients who develop STEMI. The effect of CHM on post-STEMI outcomes and especially on post-PCI outcomes is largely unknown. We sought to examine the in-hospital outcomes of patients with CHM who developed STEMI from a large national database and evaluated the impact of a PCI-based strategy compared with a conservative strategy.

Methods

The Nationwide Inpatient Sample (NIS) database, managed by the Agency for Healthcare Research and Quality (AHRQ) Healthcare Cost and Utilization Project, is the largest, all-payer database in the United States. Individual entry in the NIS provides information on patients' demographic characteristics and contains data on hospital diagnoses and procedures in the form on International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) and Clinical Classification Software codes, managed by the AHRQ. Before 2011, the NIS has been designed to represent 20% stratified sample of hospitalization of all community and nonfederal US hospitals.[8] From 2012, the NIS was significantly redesigned to represent 20% sample of all discharges of US community hospitals.[9]

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The NIS data files from January 2003 to December 2014 were used to extract the study population. All adult patients (age ≥ 18 years) who presented with STEMI were identified by using the ICD-9-CM codes. Patients who had a diagnosis of CHM, defined as chronic myelogenous leukemia, chronic lymphocytic leukemia, essential thrombocythemia, polycythemia vera, chronic monocytic leukemia, and multiple myeloma were identified by using the ICD-9-CM codes described in the Supplemental Table 1. Figure 1 demonstrates data extraction and patient selection methods.

Co-morbidities were identified by using the standard AHRQ variables based on the Elixhauser method. Patient-related co-morbidities and in-hospital characteristics were identified by using the ICD-9-CM codes. Hospital length of stay, cost of hospitalization, and postdischarge disposition were also studied. We defined patients who underwent PCI using the ICD-9-CM codes. PCIs performed within 24-hours of hospitalization were considered early PCI and those performed after 24-hours of hospitalization were classified as delayed PCI. The primary study outcome measure was in-hospital mortality.

Patients with missing information on in-hospital mortality were excluded. Baseline characteristics of the study population were analyzed. All univariate predictors of in-hospital mortality were identified. Chi-square test was used

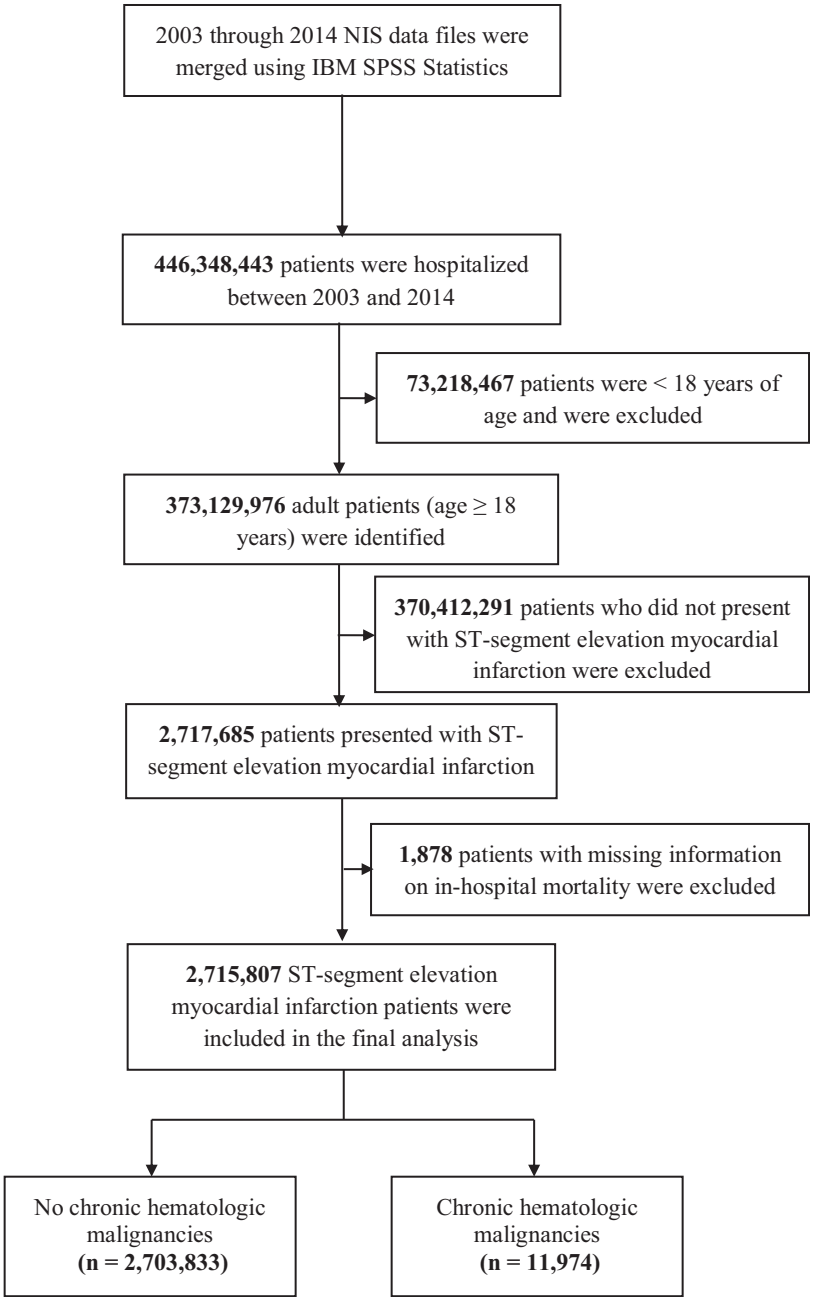

Figure 1. Data extraction and patient selection methods.

Table 1
Baseline characteristics of study population

Characteristics	Chronic hematologic malignancies		p Value
	No (n = 2,703,833)	Yes (n = 11,974)	
Age (years)	64.7 ± 14.5	73.4 ± 12.8	<0.001
Female	942,870 (34.9%)	4,801 (40.1%)	0.005
Race			<0.001
White	1,685,086 (78.8%)	8,246 (82.9%)	
Black	165,663 (7.7%)	752 (7.6%)	
Hispanic	155,578 (7.3%)	469 (4.7%)	
Asian or Pacific Islander	47,589 (2.2%)	169 (1.7%)	
Native American	11,281 (0.5%)	40 (0.4%)	
Other	72,773 (3.4%)	275 (2.8%)	
Prior stroke	37,543 (1.4%)	214 (1.8%)	<0.001
Diabetes mellitus	784,869 (29.0%)	3,324 (27.8%)	0.002
Hypertension	1,623,554 (60.0%)	7,266 (60.7%)	0.157
Congestive heart failure	642,712 (23.8%)	4,801 (40.1%)	<0.001
Peripheral vascular disease	197,046 (7.3%)	1,195 (10.0%)	<0.001
Chronic kidney disease	193,478 (7.2%)	2,319 (19.4%)	<0.001
Valvular heart disease	33,323 (1.2%)	269 (2.2%)	<0.001
Long-term use of anticoagulants	50,365 (1.9%)	465 (3.9%)	<0.001
Smoker	999,683 (37.0%)	2,883 (24.1%)	<0.001
Alcoholism	75,812 (2.8%)	182 (1.5%)	<0.001
Drug abuse	771,589 (28.5%)	1,602 (13.4%)	<0.001
Previous myocardial infarction	201,683 (7.5%)	967 (8.1%)	0.010
Previous percutaneous coronary intervention	243,916 (9.0%)	1,083 (9.0%)	0.929
Previous coronary bypass surgery	117,463 (4.3%)	724 (6.0%)	<0.001
Atrial fibrillation or atrial flutter	362,819 (13.4%)	2,650 (22.1%)	<0.001
Body mass index (kg/m^2)			
<18.5	290 (<0.1%)	0 (<0.1%)	0.257
25 to 29.9	7,306 (0.3%)	9 (0.1%)	<0.001
30 to 39.9	196,209 (7.3%)	523 (4.4%)	<0.001
≥40	59,851 (2.2%)	258 (2.2%)	0.662
Charlson comorbidity index	2.55 ± 1.85	6.69 ± 3.00	<0.001

Categorical variables are expressed as percentages, and continuous variables are expressed as mean ± standard deviation.

for categorical variables, whereas Student *t* test was used for continuous variables. Inverse probability weighting analysis was performed to adjust for differences in proximal baseline characteristics. Inverse probability matched cohorts were developed using proximal baseline variables to compare outcomes of patients with and without CHM in the overall population, in those patients who underwent PCI and in those who underwent coronary artery bypass graft (CABG) surgery. A similar inverse probability-matched cohort was extracted in CHM patient population to evaluate the effect of PCI on in-hospital mortality. Binary logistic regression model was used to adjust for postprocedural or "distal" variables, to assess the independent associations of these variables with in-hospital mortality in each of these matched cohorts. A 2-sided p value of <0.05 was considered statistically significant. The discriminatory power of the multivariate model was determined by the receiver operating characteristic-derived area under the curve. All analyses were performed in SPSS Statistics, version 24 (IBM Corporation, Armonk, New York).

Results

From January 2003 to December 2014, a total of 342,981,390 adult patients (age ≥ 18 years) were hospitalized in the United States. A total of 2,715,807 patients who presented with STEMI were included in the final analyses, of which 11,974 (0.4%) patients had a diagnosis of CHM. Table 1 demonstrates baseline patient characteristics of the 2 groups. Patients who had a diagnosis of CHM were significantly older (73.49 ± 12.76 years vs 64.75 ± 14.47 years; p <0.001) and more frequently of male gender (59.9% vs 40.1%; p <0.001). Prior stroke (1.8% vs 1.4%; p <0.001), congestive heart failure (40.1% vs 23.8%; p <0.001), peripheral vascular disease (10.0% vs 7.3%; p <0.001), chronic kidney disease (19.4% vs 7.2%; p <0.001), valvular heart disease (2.2% vs 1.2%; p <0.001), previous myocardial infarction (8.1% vs 7.5%; p = 0.01), previous cardiac surgery (6.0% vs 4.3%; p <0.001), and atrial fibrillation or atrial flutter (22.1% vs 13.4%; p <0.001) were significantly higher in patients who had CHM. Compared with patients without CHM, patients with CHM had a higher Charlson co-morbidity index (6.69 ± 3.00 vs 2.55 ± 1.85; p <0.001).

Table 2 demonstrates in-hospital characteristics of patients with and without CHM. Acute stroke (2.1% vs 1.6%; p <0.001), gastrointestinal (GI) bleeding (3.1% vs 2.4%; p <0.001), acute kidney injury (AKI) (18.9% vs 9.3%; p <0.001), cardiogenic shock (11.6% vs 8.8%; p <0.001), and vascular complications (18.5% vs 6.5%; p <0.001) were significantly higher in patients with CHM. Length of hospitalization (5.91 ± 6.47 days vs 4.64 ± 5.96

Table 2
In-hospital characteristics of study population

Characteristics	Chronic hematologic malignancies		p Value
	No (n = 2,703,833)	Yes (n = 11,974)	
Acute stroke	42,652 (1.6%)	252 (2.1%)	<0.001
Gastrointestinal bleeding	65,581 (2.4%)	368 (3.1%)	<0.001
Acute kidney injury	250,957 (9.3%)	2,261 (18.9%)	<0.001
Cardiac arrest	227,958 (8.4%)	948 (7.9%)	0.043
Cardiogenic shock	236,591 (8.8%)	1,386 (11.6%)	<0.001
Vascular complications	176,595 (6.5%)	2,219 (18.5%)	<0.001
Coronary revascularization	1,788,313 (66.1%)	5,697 (47.6%)	<0.001
Length of hospitalization (days)	4.64 ± 5.96	5.91 ± 6.47	<0.001
Cost of hospitalization ($ x 10^4)	6.50 ± 7.64	7.19 ± 9.78	<0.001
In-hospital mortality	242,165 (9.0%)	1,782 (14.9%)	<0.001
Disposition of the patient at discharge			<0.001
Routine	913,423 (68.1%)	3,546 (48.3%)	
Short-term hospital	85,565 (6.4%)	507 (6.9%)	
Intermediate care facility	117,069 (8.7%)	1,341 (18.3%)	
Home health care	101,128 (7.5%)	992 (13.5%)	
Left against medical advice	10,272 (0.8%)	19 (0.3%)	
Discharged alive, destination unknown	853 (0.1%)	0 (<0.1%)	

Categorical variables are expressed as percentages, and continuous variables are expressed as mean ± standard deviation.

days; p <0.001) and cost of hospitalization ($ × 10^4) (7.19 ± 9.78 vs 6.50 ± 7.64; p <0.001) were significantly higher in patients who had CHM. Compared with those without CHM, patients with CHM had a significantly higher unadjusted in-hospital mortality (14.9% vs 9.0%; p <0.001; Figure 2). Fewer patients with CHM underwent PCI (43.6% vs 60.1%; p <0.001), primary PCI (28.6% vs 40.2%; p <0.001), and delayed PCI (15.0% vs 19.9%; p <0.001) compared with those without CHM (Figure 3). Patients with CHM had a higher probability of requiring postdischarge rehabilitation unit care (18.3% vs 8.7%; p <0.001) and home health care (13.5% vs 7.5%; p <0.001).

Univariate predictors of in-hospital mortality are shown in Table 3. Acute stroke (5.4% vs 1.2%; p <0.001), GI bleeding (6.2% vs 2.1%; p <0.001), AKI (32.3% vs 7.1%; p <0.001), cardiac arrest (35.5% vs 5.8%; p <0.001), cardiogenic shock (36.4% vs 6.0%; p <0.001), vascular complications (10.3% vs 6.2%; p <0.001), and CHM (0.7% vs 0.4%; p <0.001) were significantly associated with a higher in-hospital mortality.

Table 4 depicts inverse probability weighting-adjusted binary logistic regression model. Independent predictors of in-hospital mortality were acute stroke (odds ratio [OR] = 3.08, 95% confidence interval [CI] = 2.99 to 3.16;

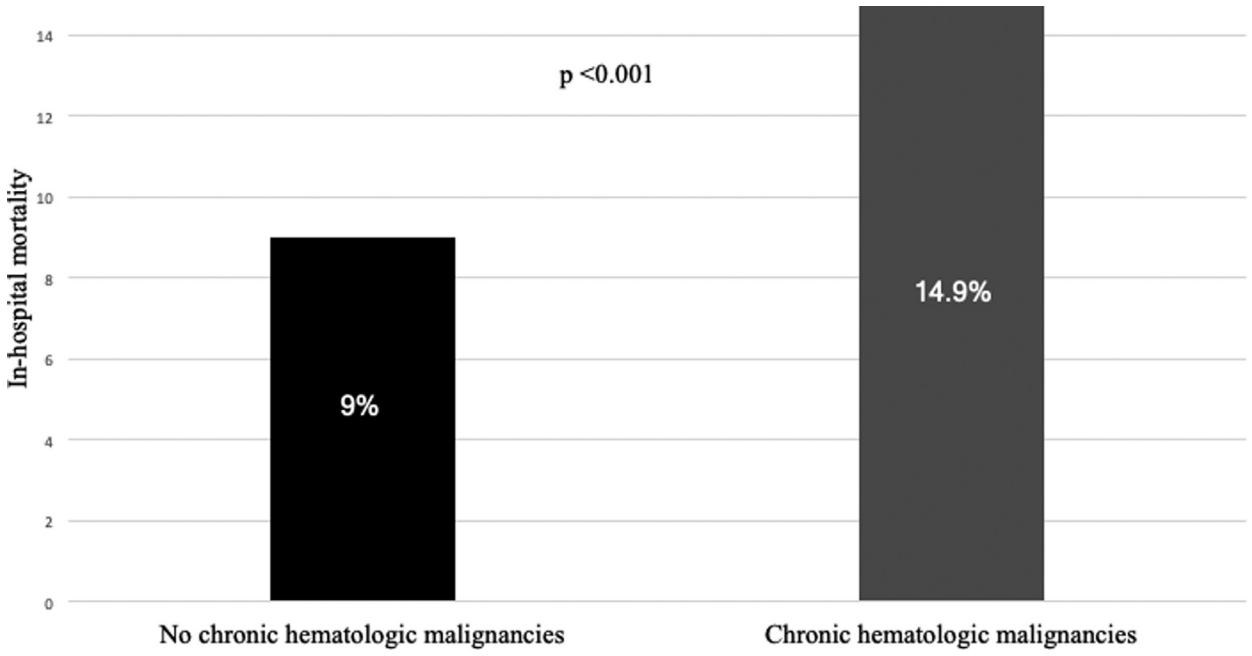

Figure 2. Comparative in-hospital mortality outcomes in patients with and without chromic hematologic malignancies.

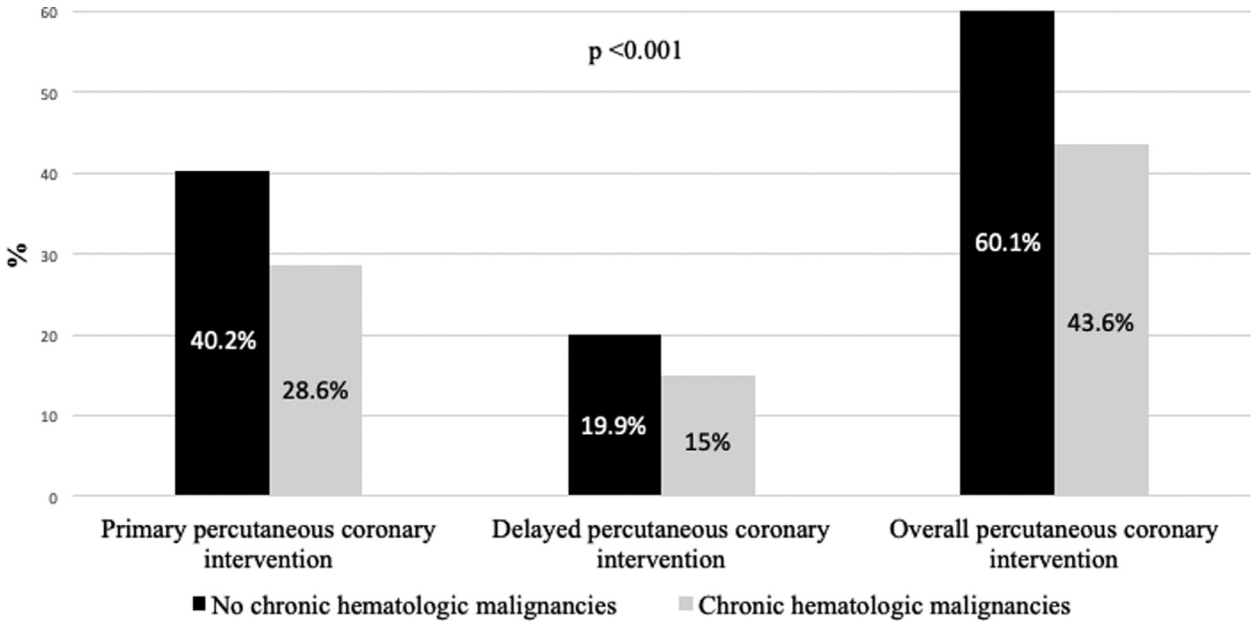

Figure 3. Utilization of PCI in STEMI patients with and without chronic hematologic malignancies.

p <0.001), GI bleeding (OR = 1.51, 95% CI = 1.47 to 1.55; p <0.001), AKI (OR = 2.52, 95% CI = 2.49 to 2.56; p <0.001), cardiac arrest (OR = 8.68, 95% CI = 8.57 to 8.80; p <0.001), cardiogenic shock (OR = 6.59, 95% CI = 6.50 to 6.68; p <0.001), and vascular complications (OR = 1.15, 95% CI = 1.08 to 1.21; p <0.001). CHM did not independently predict a higher in-hospital mortality (OR = 1.02, 95% CI = 0.96 to 1.09; p = 0.461). Coronary revascularization (PCI or CABG surgery) was associated with a significant and sizeable reduction in in-hospital mortality (OR = 0.16, 95% CI = 0.15 to 0.16; p<0.001). The multivariate model demonstrated good discrimination (c-statistic = 0.89).

Supplemental Tables 2 to 5 show baseline characteristics, in-hospital outcomes, univariate and independent predictors of mortality in the inverse probability-weighted cohort of STEMI patients with CHM with or without PCI, respectively. In patients with CHM who presented with STEMI, PCI was found to be associated with a significant reduction in in-hospital mortality compared with conservative therapy (OR = 0.22; 95% CI = 0.18 to 0.27; p <0.001; c-statistic = 0.81). Supplemental Tables 6 to 8 depict baseline characteristics, in-hospital outcomes, univariate and independent predictors of mortality in the inverse probability-weighted cohort of STEMI patients who underwent primary PCI with or without CHM, respectively. CHM was not independently associated with in-hospital mortality in this cohort (OR = 0.84; 95% CI = 0.69 to 1.09; p = 0.098; c-statistic = 0.92).

Table 4
Independent predictors of in-hospital mortality

Independent variables	In-hospital mortality	
	OR (95% CI)	p Value
Chronic hematologic malignancies	1.02 (0.96-1.09)	0.461
Acute stroke	3.08 (2.99-3.16)	<0.001
Gastrointestinal bleeding	1.51 (1.47-1.55)	<0.001
Acute kidney injury	2.52 (2.49-2.56)	<0.001
Cardiac arrest	8.68 (8.57-8.80)	<0.001
Cardiogenic shock	6.59 (6.50-6.68)	<0.001
Vascular complications	1.15 (1.08-1.21)	<0.001
Coronary revascularization	0.16 (0.15-0.16)	<0.001

CI = confidence interval; OR = odds ratio.

Table 3
Univariate predictors of in-hospital mortality

Characteristics	Survived (n = 2,471,860)	Died (n = 243,947)	p Value
Acute stroke	29,644 (1.2%)	13,260 (5.4%)	<0.001
Gastrointestinal bleeding	50,743 (2.1%)	15,206 (6.2%)	<0.001
Acute kidney injury	174,312 (7.1%)	78,906 (32.3%)	<0.001
Cardiac arrest	142,227 (5.8%)	86,679 (35.5%)	<0.001
Cardiogenic shock	149,138 (6.0%)	88,839 (36.4%)	<0.001
Vascular complications	153,596 (6.2%)	25,218 (10.3%)	<0.001
Coronary revascularization	1,715,295 (69.4%)	78,715 (32.3%)	<0.001
Chronic hematologic malignancies	10,192 (0.4%)	1,782 (0.7%)	<0.001

Discussion

Our study shows that presence of CHM is not an independent predictor of worse outcomes in patients presenting with STEMI regardless of treatment strategy. Similar to patients without CHM, those with CHM and STEMI who underwent PCI have lower in-hospital mortality compared with those managed conservatively. In-hospital mortality of patients with STEMI and CHM who underwent CABG is also similar to those with STEMI without CHM.

Unadjusted in-hospital outcomes of STEMI patients with CHM were worse compared with STEMI patients without CHM. This was likely driven by older age and a higher prevalence of adverse nonmalignant co-morbidities in STEMI patients with CHM. CHM patients were also more likely to develop AKI, GI bleeding, and major vascular access site complications during the hospitalization compared with those without CHM. As seen in other STEMI cohorts, post-PCI outcomes appear to be associated with these well-known nonmalignant co-morbidities and complications. Our results show that STEMI patients with CHM had a higher cost of hospitalization, hospital length of stay, as well as need for postdischarge rehabilitation and home health nursing care. This finding is also likely related to a higher prevalence of co-morbid conditions in this patient subset.

Historically, a diagnosis of CHM has been felt to impart a major prognostic disadvantage and hence aggressive management when they develop STEMI is deemed futile. With improving treatment, the prognosis of CHM has improved, hence magnifying the role of STEMI as the prime driver of short-term and long-term adverse outcomes in this cohort. The patient with CHM is typically felt to be marred with multiple conditions that could adversely affect the outcome of PCI. These include presence of a hypercoagulable as well as hemorrhagic tendencies. The blood dyscrasias associated with CHM, such as anemia[10] and thrombocytopenia,[11] have been well known to adversely impact prognosis in PCI patients. The improved outcomes observed with PCI in our cohort, likely reflect the effect of improvements in stent technology, antithrombotic pharmacotherapy and procedural changes such as better access site choice in the contemporary era attenuating the adverse influence of the systemic milieu in patients with CHM. Attempts to mitigate consequences of interruption of dual antiplatelet therapy, which is expected to be more likely in CHM patients, such as intravascular ultrasound-guided stenting to prevent under deployment and use of the latest generation stents associated with the lowest rates of stent thrombosis would be intuitive to ensure durable outcome benefit of PCI in this complex cohort of patients.

Based on our results, CHM patients presenting with STEMI should be treated with similar treatment strategies as those without CHM, including revascularization if indicated, as there appears to be a sizeable outcome advantage with this approach and no harmful effect of CHM on these outcomes.

Our results are limited to in-hospital outcomes and hence long-term efficacy and safety of PCI or CABG in STEMI patients with CHM cannot be commented on from this analysis. Being an observational retrospective database, the NIS is subject to confounding variables. Inverse probability weighting may offset the effects of known confounders although residual confounding likely exists. The NIS is an administrative database and is subject to coding errors. Since individual entry in NIS represents a hospital discharge, results might be different if individual patient data were available. Lack of granular details, such as procedural and laboratory data as well as details of pharmacotherapy further limit the analyses.

In conclusion, in patients presenting with STEMI, an existing diagnosis of CHM does not appear to be independently associated with a higher in-hospital mortality. These patients, although with more co-morbidities and a higher likelihood of in-hospital complications, derive sizeable outcome benefit from acute reperfusion compared with conservative care, similar to those without CHM.

Disclosures

The authors have no conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.04.049.

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