Incidence, Predictors, and Outcomes of Major Bleeding Among Patients Hospitalized With Acute Heart Failure

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Acute heart failure (AHF) is a common etiology of hospitalization and is associated with morbidity, including bleeding. In this study, the authors sought to assess the incidence, types, and associates of major bleeding in patients hospitalized with AHF. The National Inpatient Sample from October 2015 to December 2018 was used to identify patients with AHF. The incidence of common bleeding etiologies, and patient demographics, co-morbidities, associated acute cardiac diagnoses, and invasive procedures, were identified. The multivariable logistic regression was used to identify predictors of bleeding and the association of bleeding episodes with inpatient mortality. During the study period, 1,106,634 patients were admitted with a primary diagnosis of AHF, of whom 58,955 (5.3%) had an episode of bleeding. Common bleeding sources were gastrointestinal (25.7%), hematuria (24%), respiratory (23.6%), and procedure-related bleeding (2.5%). Major bleeding was more common in patients with AHF with preserved ejection fraction (odds ratio 1.14, confidence interval 1.12 to 1.16, p <0.001) versus AHF with reduced ejection fraction and in men (odds ratio 1.3, confidence interval 1.29 to 1.31, p <0.001). Major bleeding was associated with higher mortality (7.0% vs 2.4%, p <0.001), longer length of stay (7 vs 4 days, p <0.001), and higher inpatient costs ($49,658 vs $27,636, p <0.001). In conclusion, major bleeding occurs in 5.3% of patients hospitalized with AHF and is associated with higher inpatient mortality and costs and longer length of stay. **(Am J Cardiol 2023;191:59−65)**

Acute heart failure (AHF) is a common cause of hospitalization and is associated with significant inpatient morbidity. A potential source of morbidity among patients hospitalized with AHF is major bleeding. Patients with AHF may have numerous risk factors for major bleeding. These include concomitant conditions that may be present in patients with AHF, such as atrial fibrillation, anemia, and renal dysfunction, which are associated with increased bleeding risk.[1] Patients with AHF may also be prescribed high-risk medications, such as anticoagulants and antiplatelet agents, and may need invasive procedures. A history of heart failure (HF) has been identified as a risk factor for bleeding in patients presenting with acute myocardial infarction (AMI),[2,3] and AHF is a component of the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines) score. to predict bleeding in patients with AMI.[4] Although there is a significant number of studies on the bleeding risks and outcomes associated with other common causes of cardiovascular hospitalization, including atrial fibrillation and AMI,[1,2,5−9] there are limited data on major bleeding and its implications among patients hospitalized with AHF. Data are also lacking on the risks of bleeding in patients with AHF with reduced ejection fraction (HFrEF) versus preserved ejection fraction (HFpEF) and among patients with AHF who underwent invasive procedures. With this background, we sought to evaluate the incidence, etiology, and outcomes associated with major bleeding among patients hospitalized with AHF from a large national dataset.

Methods

The National Inpatient Sample (NIS) is the largest all-payer inpatient health care database in the United States. The dataset is developed by the Healthcare Cost and Utilization Project and sponsored by the Agency for Healthcare Research and Quality.[10] The NIS dataset contains hospital information on 7 to 8 million yearly hospital discharges. Since 2012, the NIS samples discharges from participating

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hospitals, approximating a 20% stratified sample of all discharges from US community hospitals.

We analyzed all adult patients (aged ≥18 years) hospitalized with a principal diagnosis of AHF from October 1, 2015 through December 2018. Patient and procedural characteristics, including for AHF diagnoses, were extracted using International Classification of Diseases, Tenth Revision codes provided in Supplementary Table 1. Information on patient demographics was recorded for each hospital discharge, including age, race, gender, admission day (weekend or weekday), expected primary payer, and median household income. Missing records for key characteristics, including age, gender, elective admission, and mortality status, were excluded from analysis (Figure 1 for the study flow diagram). Patients aged <18 years and elective admissions were also excluded from the analysis. Each discharge record contains information on up to 30 diagnoses. International Classification of Diseases, Tenth Revision codes were used to identify procedural information during hospitalization, including invasive coronary angiography, percutaneous coronary intervention (PCI), implantable cardioverter-defibrillator (ICD), and cardiac resynchronization therapy (CRT), and the use of mechanical ventilation, circulatory support, and palliative care consultation.

The primary outcome measured was major in-hospital bleeding. Major bleeding events were defined as a composite of gastrointestinal, respiratory tract, hematuria, retroperitoneal, intracranial, periprocedural, other, and unspecified, with using International Classification of Diseases, Tenth Revision codes shown in Supplementary Table 1. Other bleeding denotes bleeding sources not otherwise noted, such as hemothorax, uterine/vaginal bleeding, and others, as shown in Supplementary Table 1. We also evaluated in-hospital mortality, length of stay (LOS), inpatient costs, and discharge destination. We performed a sensitivity analysis using a more inclusive definition of major bleeding, adding receipt of blood transfusion to the definition of major bleeding.

Continuous variables are presented as a median and interquartile range because of skewed data, and categorical data are presented as percentages and frequencies. Categorical variables were compared using the Pearson chi-square test, whereas continuous variables were compared using the Student's t test or the Mann−Whitney U test. Sampling weights were used to calculate the estimated total number of discharges specified by the Agency for Healthcare Research and Quality. Multivariable logistic regression models were used to examine the association between demographics, co-morbidities, in-hospital procedures, and major bleeding events, and the association between gender and AHF subtype (HFrEF and HFpEF) and major bleeding events; all expressed as odds ratios (ORs) with corresponding 95% confidence intervals (CIs). The models were

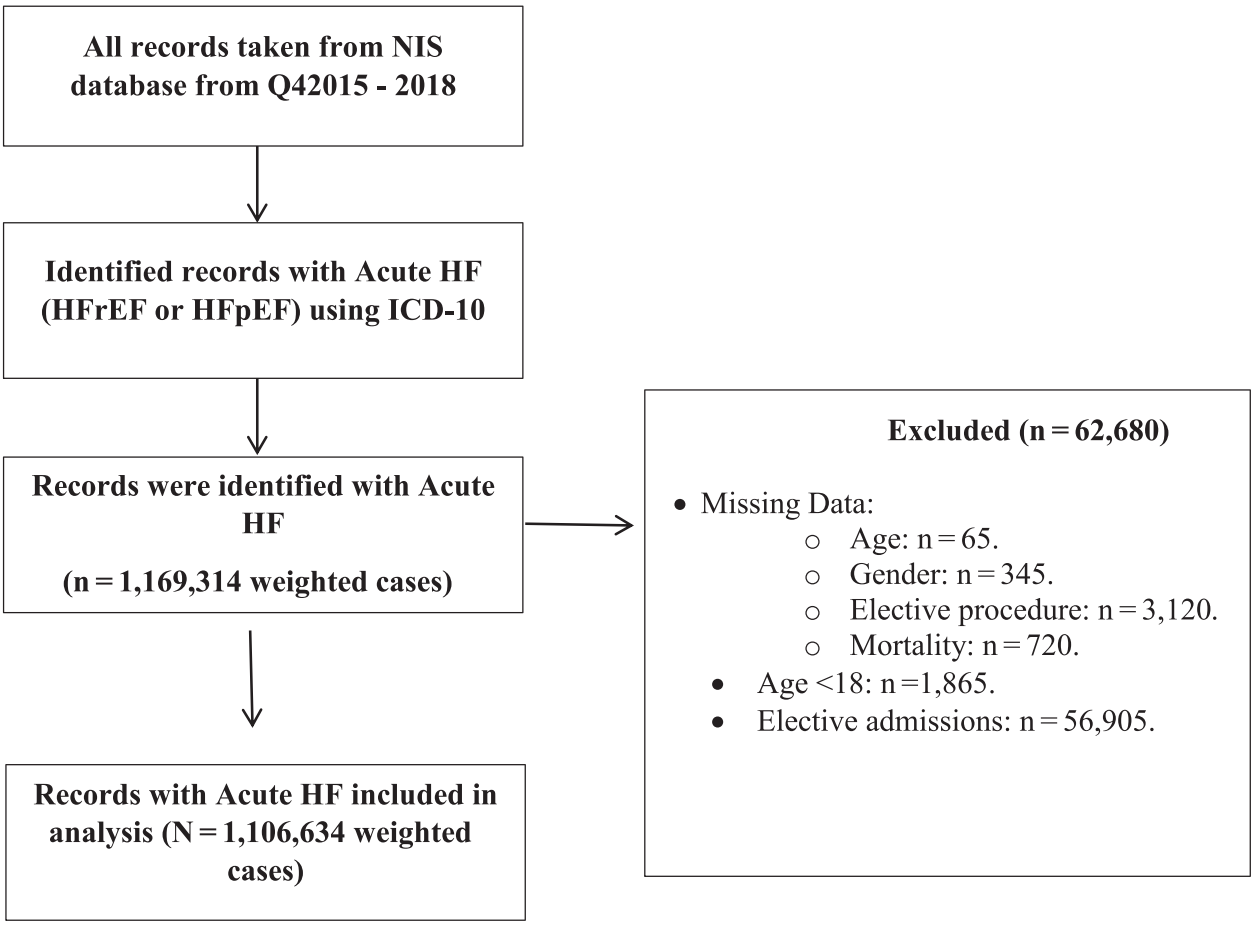

Figure 1. Flow Diagram of study population.

adjusted for baseline differences between the groups, controlling for the following covariates: age, gender, HF type, race, median zip income, weekend admission, expected primary payer, hospital bed number, region and location/teaching status, AMI, cardiogenic shock, ventricular fibrillation, ventricular tachycardia, atrial fibrillation, chronic ischemic heart disease, peripheral vascular disease (PVD), cerebrovascular disease, dyslipidemia, hypertension, diabetes mellitus, valvular heart disease, chronic lung disease, smoking status, chronic renal failure, chronic liver disease, thrombocytopenia, anemia, coagulopathies, dementia, malignancies, coronary angiography, PCI, and CRT/ICD implantation. All statistical analyses were performed on IBM SPSS version 26 (IBM Corp., Armonk, NY, USA). Statistical significance was set at the 2-tailed 0.05 level without multiplicity adjustment.

Results

During the study period, 1,106,634 patients were admitted with a primary diagnosis of AHF, 58,955 of whom (5.3%) had an episode of major bleeding during the hospitalization (Table 1). The most common types of major bleeding were gastrointestinal bleeding (1.6% of patients), hematuria (1.3%), respiratory tract bleeding (1.3%), and unspecified bleeding (1.1%), with other major bleeding types, including intracranial bleeding (0.1%), procedure-related bleeding (0.1%), retroperitoneal bleeding (<0.1%), and other bleeding (0.2%), occurring less commonly (Supplementary Table 2). Patients who had an episode of major bleeding were more likely to have cardiovascular comorbidities, including ischemic heart disease (56.2% vs 52.0%, p <0.001), cerebrovascular disease (5.2% vs 4.2%, p <0.001), valvular disease (30.6% vs 26.3%, p <0.001), PVD (11.6% vs 10.2% p <0.001), and atrial fibrillation/flutter (55.8% vs 45.9%, p <0.001) and noncardiovascular comorbidities, including chronic renal failure (50.2% vs 43.0%, p <0.001), thrombocytopenia (11.8% vs 5.4%, p <0.001), coagulopathy (5.9% vs 1.5%, p <0.001), and chronic liver disease (2.5% vs 1.7%, p <0.001). Pre-existing anemia was more common among patients who had an episode of major bleeding (32.2% vs 31.6%, p = 0.02). Patients who had an episode of major bleeding were also more likely to have solid malignancy (4.1% vs 2.7%, p <0.001), hematologic malignancy (2.3% vs 1.8%, p <0.001), and metastatic cancer (1.5% vs 1.1%, p <0.001). Major bleeding was also more common among patients who had an AMI (6.8% vs 3.8%, p <0.001), cardiac arrest (2.0% vs 0.5%, p <0.001), and ventricular arrhythmias, including ventricular tachycardia (9.1% vs 5.3%, p <0.001)

Table 1
Baseline, clinical characteristics, in-hospital procedures and outcomes, stratified by occurrence of major bleeding event

	Whole cohort	No major bleeding	Had major bleeding	p Value*
Number of weighted records (%)	1,106,634	1,047,679 (94.7%)	58,955 (5.3%)	
Age (years), median (IQR)	74 (62,84)	74 (62,84)	74 (64,83)	<0.001
Females, %	48.2%	48.5%	42.3%	<0.001
Race				<0.001
White	69.3%	69.1%	71.9%	
Black	18.9%	19.0%	16.8%	
Hispanic	7.2%	7.2%	6.4%	
Asian/pacific islander	2.0%	2.0%	2.2%	
Native American	0.5%	0.5%	0.5%	
Other	2.2%	2.2%	2.3%	
Hospital location				<0.001
Northeast	20.9%	20.9%	20.8%	
Midwest	23.4%	23.3%	25.2%	
South	39.0%	39.0%	38.4%	
West	16.7%	16.7%	15.5%	
Hospital size				<0.001
Small	20.0%	20.2%	16.8%	
Medium	29.5%	29.6%	27.5%	
Large	50.5%	50.2%	55.7%	
Hospital location/teaching status				<0.001
Rural	11.3%	11.4%	9.1%	
Urban non-teaching	27.1%	27.3%	23.5%	
Teaching	61.7%	61.3%	67.4%	
Weekend admission	24.0%	24.0%	23.7%	0.22
Median ZIP income				<0.001
1st quartile	33.0%	33.1%	31.2%	
2nd quartile	26.2%	26.2%	26.1%	
3rd quartile	23.2%	23.2%	23.6%	
4th quartile	17.7%	17.6%	19.1%	
Expected primary payer				<0.001
Medicare	73.1%	73.0%	75.3%	

(*continued*)

Table 1 (***Continued***)

	Whole cohort	No major bleeding	Had major bleeding	p Value*
Medicaid	10.7%	10.8%	8.8%	
Private	11.6%	11.5%	12.2%	
Uninsured	2.7%	2.7%	2.0%	
No charge	0.2%	0.2%	0.1%	
Other	1.7%	1.7%	1.5%	
Clinical characteristics				
HFrEF	60.3%	60.3%	59.6%	<0.001
Acute MI	4.0%	3.8%	6.8%	<0.001
Cardiac arrest	0.7%	0.5%	2.0%	<0.001
Ventricular fibrillation	0.3%	0.3%	1.1%	<0.001
Ventricular tachycardia	5.5%	5.3%	9.1%	<0.001
Cardiogenic shock	2.4%	2.0%	8.6%	<0.001
Length of stay, days, median (IQR)	4 (3,6)	4 (2,6)	7 (4,12)	<0.001
Total charge, $, median (IQR)	28,339 (16,766−50,513)	27,636 (16,451−48,642)	49,658 (26,608−112,612)	<0.001
Co-morbidities				
Ischemic heart disease	52.2%	52.0%	56.2%	<0.001
Cerebrovascular disease	4.2%	4.2%	5.2%	<0.001
Valvular disease	26.5%	26.3%	30.6%	<0.001
Atrial fibrillation/flutter	46.4%	45.9%	55.8%	<0.001
Hypertension	75.3%	75.4%	72.7%	<0.001
Dyslipidemia	48.9%	49.0%	46.8%	<0.001
Diabetes mellitus	44.6%	44.7%	42.3%	<0.001
Smoking	42.6%	42.8%	39.9%	<0.001
Peripheral vascular disease	10.3%	10.2%	11.6%	<0.001
Chronic lung disease	41.0%	41.1%	40.5%	0.004
Chronic renal failure	43.4%	43.0%	50.2%	<0.001
Obesity	22.7%	22.8%	21.3%	<0.001
Anemia	31.6%	31.6%	32.2%	0.02
Thrombocytopenia	5.8%	5.4%	11.8%	<0.001
Coagulopathy	1.8%	1.5%	5.9%	<0.001
Dementia	8.4%	8.5%	8.3%	0.16
Chronic liver disease	1.8%	1.7%	2.5%	<0.001
Solid malignancy	2.8%	2.7%	4.1%	<0.001
Hematologic malignancies	1.9%	1.8%	2.3%	<0.001
Metastatic cancer	1.1%	1.1%	1.5%	<0.001
In-hospital procedures				
Coronary angiography	7.7%	7.5%	11.0%	<0.001
PCI	1.0%	1.0%	1.9%	<0.001
CRT/ICD implantation	1.0%	1.0%	1.3%	<0.001
Mechanical ventilation	2.1%	1.7%	8.0%	<0.001
Circulatory support	0.5%	0.3%	3.9%	<0.001
Palliative consultation	4.5%	4.3%	7.9%	<0.001
Blood transfusion	3.1%	2.3%	16.7%	<0.001
In-hospital mortality	2.7%	2.4%	7.0%	<0.001

* p-Value for major bleeding vs no major bleeding.

HF = heart failure; IQR = interquartile range; MI = myocardial infarction.

and ventricular fibrillation (1.1% vs 0.3%, p <0.001). Patients with an episode of major bleeding were more likely to receive a blood transfusion (16.7 vs 2.3%, p <0.001). In addition, major bleeding was more common among patients who underwent invasive procedures, including coronary angiography (11.0% vs 7.5%, p <0.001), PCI (1.9% vs 1.0%, p <0.001) and implantation of a pacemaker or defibrillator (1.3% vs 1.0%, p <0.001), and mechanical ventilation (8.0% vs 1.7%, p <0.001).

The independent co-morbidity predictors of major bleeding are shown in Table 2. The key predictors of bleeding included obesity (OR 1.05, 1.03 to 1.07, p <0.001), ischemic heart disease (OR 1.1, 1.08 to 1.12, p < 0.001), cerebrovascular disease (OR 1.18, 1.13 to 1.22, p < 0.001), atrial fibrillation/flutter (OR 1.45, 1.42 to 1.48, p <0.001), thrombocytopenia (OR 1.51, 1.46 to 1.55, p <0.001), solid malignancy (OR 1.33, 1.27 to 1.40, p <0.001), coagulopathy (OR 2.68, 2.57 to 2.79, p <0.001), and anemia (OR 1.02, 1.01 to 1.04, p = 0.02). Acute cardiac conditions independently associated with major bleeding included AMI (OR 1.53, 1.47 to 1.58, p <0.001), cardiac arrest (OR 2.03, 1.89 to 2.18, p <0.001) and cardiogenic shock (OR 2.99, 2.88 to 3.10, p <0.001). The performance of coronary angiography (OR 1.42, 1.38 to 1.47, p <0.001) and PCI (OR 1.19, 1.11 to 1.28, p <0.001) were also associated with bleeding events. The male gender (OR 1.3, 1.28 to 1.31, p

Table 2
Predictors of in-hospital major bleeding

	OR (95% CI)	p Value
Age (years),	1.0 (0.99−1.01)	0.89
Male	1.3 (1.28−1.31)	<0.001
HFpEF	1.14 (1.12−1.16)	<0.001
Acute MI	1.53 (1.47−1.58)	<0.001
Cardiac arrest	2.03 (1.89−2.18)	<0.001
Ventricular fibrillation	1.34 (1.21−1.48)	<0.001
Ventricular tachycardia	1.36 (1.32−1.41)	<0.001
Cardiogenic shock	2.99 (2.88−3.1)	<0.001
Ischemic heart disease	1.1 (1.08−1.12)	<0.001
Cerebrovascular disease	1.18 (1.13−1.22)	<0.001
Valvular disease	1.08 (1.06−1.1)	<0.001
Atrial fibrillation/flutter	1.45 (1.42−1.48)	<0.001
Hypertension	0.89 (0.87−0.91)	<0.001
Dyslipidemia	0.9 (0.88−0.92)	<0.001
Diabetes mellitus	0.9 (0.88−0.91)	<0.001
Smoking	0.9 (0.89−0.92)	<0.001
Peripheral vascular disease	1.03 (1.0−1.05)	0.06
Chronic lung disease	1.03 (1.01−1.05)	0.03
Chronic renal failure	0.99 (0.97−1.01)	0.38
Obesity	1.05 (1.03−1.07)	<0.001
Anemia	1.02 (1.01−1.04)	0.02
Thrombocytopenia	1.51 (1.46−1.55)	<0.001
Coagulopathy	2.68 (2.57−2.79)	<0.001
Dementia	0.97 (0.94−1.0)	0.04
Chronic liver disease	1.03 (0.98−1.09)	0.28
Solid malignancy	1.33 (1.27−1.4)	<0.001
Hematologic malignancies	0.93 (0.88−0.99)	0.02
Metastatic cancer	0.91 (0.84−0.98)	0.02
In-hospital procedures		
Coronary angiography	1.42 (1.38−1.47)	<0.001
PCI	1.19 (1.11−1.28)	<0.001
CRT/ICD implantation	1.02 (0.95−1.11)	0.57

<0.001) and HFpEF (vs HFrEF; OR 1.14, 1.12 to 1.16, p <0.001) were also associated with a higher risk of major bleeding.

The differences in bleeding types by gender are shown in Supplementary Figure 1. Men were more likely than women to experience hematuria (1.7% vs 0.8%, p <0.001) and respiratory tract bleeding (1.5% vs 1.0%, p <0.001), which contributed to the overall higher bleeding rates in men. There were no significant differences in the incidence of "other" bleeding types, which include vaginal and uterine bleeding, among other etiologies, between men and women (0.2% vs 0.3%, p = 0.06); although, these bleeding types were overall rare.

Compared with patients with HFrEF, those with HFpEF were more likely to have gastrointestinal bleeding as an etiology of major bleeding (28.0% vs 24.1% of total bleeds, p <0.001) and less likely to have procedure-related bleeding (1.3% vs 3.3%, p <0.001), as shown in Supplementary Table 3. This was partly due to fewer procedures, including coronary angiography (3.7% vs 10.4%, p <0.001), PCI (0.5% vs 1.4%, p <0.001), and ICD/CRT (0.1% vs 1.7%, p <0.001), performed among the HFpEF cohort. However, among those patients who did undergo invasive procedures, the rate of major bleeding was similar between patients with HFpEF and HFrEF for those who underwent coronary angiography (0.8% vs 0.8%, p = 0.76) and PCI (1.8% vs 1.5%, p = 0.27) but higher for rare patients with HFpEF among those who underwent CRT/ICD (2.6% vs 0.9%, p <0.001; Supplementary Table 4).

Table 3
Unadjusted and adjusted OR of Patients with major bleeding for In-hospital mortality

	Unadjusted		Adjusted*	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Entire cohort	3.03 (2.93−3.14)	<0.001	1.79 (1.72−1.87)	<0.001
HFrEF	3.27 (3.13−3.4)	<0.001	1.74 (1.65−1.83)	<0.001
HFpEF	2.65 (2.49−2.81)	<0.001	1.89 (1.76−2.03)	<0.001

* Adjusted for age, gender, and HF type, race, median zip income, expected primary payer, weekend admission, hospital bed size, region and location/teaching status, acute MI, cardiogenic shock, VF, VT, AF, chronic ischemic heart disease, cerebrovascular disease, PVD, hypertension, dyslipidemias, diabetes mellitus, valvular heart disease, smoking status, chronic lung disease, chronic renal failure, chronic liver disease, anemia, thrombocytopenia, coagulopathies, dementia malignancies, coronary angiography, PCI, and CRT/ICD implantation.
Reference = no major bleeding.

Major bleeding was associated with higher mortality (7.0% vs 2.4%, p <0.001), longer LOS (7 vs 4 days, p <0.001), and higher inpatient costs ($49,658 vs $27,636, p <0.001). In the multivariable analyses, major bleeding was associated with a significantly higher rate of inpatient mortality OR 1.79 (1.72 to 1.87, p <0.001; Table 3). Among the bleeding types, patients with gastrointestinal bleeding had an inpatient mortality of 9.7%, procedure-related bleeding had a mortality of 14.9%, intracranial bleeding had a mortality of 23.9%, and patients with retroperitoneal bleeding had a mortality of 17.3%. In contrast, other bleeding sites had a lower mortality rate (Supplementary Table 2). Patients with an episode of bleeding were also less likely to be discharged home (33.9% vs 50.4%, p <0.001) and more likely to be discharged to a nursing care facility (29.0% vs 19.5%, p <0.001), as shown in Supplementary Figure 2.

A sensitivity analysis, to reveal independent co-morbidity predictors of a more inclusive definition of major bleeding (including blood transfusion receipt), is presented in Supplementary Table 5. Anemia was a strong predictor of major bleeding that included receipt of blood transfusion in definition (OR 5.45, 95% CI 5.37 to 5.54, p <0.001), whereas chronic renal failure, chronic liver disease, and PVD were found to be predictors only for major bleeding definition that included the transfusion end point (OR 1.11 [95% CI 1.09 to 1.13], 1.15 [95% CI 1.1 to 1.21], and 1.05 [95% CI 1.03 to 1.07], respectively; all p <0.001).

Discussion

This analysis of incidence, predictors, and outcomes associated with significant bleeding among patients hospitalized with AHF demonstrates several important findings. Major bleeding occurred in 5.3% of patients hospitalized with AHF and was more common in patients with HFpEF than in patients with HFrEF. The gastrointestinal, urinary, and respiratory tract were the most common etiologies of

major bleeding, with procedural and intracranial bleeding occurring less frequently. The independent predictors of major bleeding included common cardiac and noncardiac co-morbidities, associated cardiac conditions, such as AMI and cardiogenic shock, and the use of invasive procedures. Major bleeding was associated with significant increases in inpatient mortality, higher LOS, and higher inpatient costs. These results have important clinical implications for the care of patients admitted with AHF as they identify risk factors and outcomes associated with major bleeding.

Our findings add to the previous literature on bleeding among patients hospitalized for cardiovascular conditions or who underwent cardiovascular procedures. All-cause bleeding was noted in 7.5% of patients presenting with AMI, with vital contributing factors of cardiac arrest, cardiogenic shock, STEMI, HF, anemia, tachycardia, obesity, and chronic kidney disease being associated with higher risk.[2] The CRUSADE registry of high-risk patients with AMI reported major bleeding in 9.4% of patients, with both previous HF and AHF identified as predictors of bleeding.[4] Bleeding rates among patients who underwent PCI were reported to be 5.8%, at risk factors of age, chronic kidney disease, shock, cardiac arrest, female gender, abnormal hemoglobin, STEMI, and PCI status associated with higher risk.[5] Among patients presenting with AMI, those with a history of pre-existing HFpEF and HFrEF had a higher rate of major bleeding than patients without HF.[3] Patients admitted for transcatheter aortic valve replacement (TAVR) were reported to have bleeding rates of 6.6%, with HF being an independent risk factor.[8] Bleeding rates were also higher in patients presenting with AMI and atrial fibrillation based on the CHADSVASC score, with the HF component of the score independently associated with higher inpatient bleeding risk.[6] Prior studies have also focused on gastrointestinal bleeding among patients admitted with atrial fibrillation[7] and hypertrophic cardiomyopathy,[11] with both studies demonstrating approximately a 5% bleeding rate.

Our study expands on these previous studies of other cardiovascular conditions, with specific attention to patients with AHF. Patients with AHF experience bleeding rates which approach although may be lower than other high-risk cohorts including patients with AMI, PCI, and invasive procedures such as TAVR. Although patients with HF have a high co-morbidity burden, including co-morbidities that have been associated with major bleeding,[1] there are several reasons why bleeding rates among patients with AHF may be lower than among patients hospitalized for other cardiovascular conditions. Patients with pre-existing HF may be less likely to undergo invasive procedures, even for conditions such as AMI,[3] which may decrease the propensity for bleeding. However, in the current analysis, bleeding was more common in patients who underwent invasive procedures, implying that a particular focus on the AHF population who underwent procedures may be prudent. Pharmacologic therapy in patients with AHF may also differ significantly from patients with AMI, atrial fibrillation, or patients who experience invasive cardiac procedures, with less use of antiplatelet and anticoagulation therapies in the HF population in the absence of other indications. This may be supported by higher bleeding rates among patients with AHF who have a history of atherosclerotic diseases such as ischemic heart disease, cerebrovascular disease, peripheral arterial disease, and atrial fibrillation as these patients are more likely to be on secondary prevention antiplatelet or anticoagulation therapies.

In the present study, the bleeding risk was higher in men than in women. The higher risk in men was predominantly due to a higher incidence of hematuria and respiratory tract bleeding, with no significant difference in other bleeding types. Other genitourinary bleeding, including vaginal and uterine bleeding, was rare in this cohort. The reasons for the higher incidence of major bleeding in men are unclear and deserve further investigation. Possible explanations may include higher predisposing risk factors to respiratory bleeding (such as smoking) and more complex urinary catheter placement requirements in men. While higher bleeding in men identified in this cohort is contrary to previous studies in some populations such as AMI, other cohorts of PCI and atrial fibrillation patients demonstrated no difference in overall bleeding or similarly found higher bleeding rates in men.[12,13]

Appreciating the risk factors associated with major bleeding among patients with AHF is essential given that such bleeding is associated with longer LOS, higher costs, and increased mortality. The clinically important contributors to major bleeding among patients with AHF include co-morbidities, which may increase bleeding directly or be associated with therapies, including antiplatelet and anticoagulation help, which may be associated with bleeding risk. Patients with coagulopathy, thrombocytopenia, chronic liver disease, and other co-morbidities may require extra attention for co-morbidity management and potentially reduce the risks of bleeding complications. Similarly, patients presenting after cardiac arrest or in cardiogenic shock and those who underwent invasive procedures may benefit from an increased focus on bleeding complications, which may include gastrointestinal bleeding prophylaxis and close management of coagulopathy because of underlying co-morbidities or medication use. A focus on risk factors associated with major bleeding may help identify pathways to inpatient mortality, reduce LOS, and lead to significant reduction in system costs related to bleeding in AHF hospitalizations.[14] Bleeding reduction is a common focus among patients who underwent invasive cardiac procedures, including PCI and TAVR, and similar efforts may be needed in the AHF population.

The present analysis has important limitations, including those inherent to the use of the NIS. The data in the NIS are based on physician-entered coding and is therefore dependent on the accuracy of the entered data. Necessary granularity of the data, including etiology of HF, ejection fraction, co-morbidity severity, and duration, is not available in this dataset. This may be important for the severity of HF, and for determining the accuracy of HFrEF versus HFpEF as key diagnoses. Similarly, concomitant medication use and laboratory values are not available. The definitions of bleeding may vary between this and other cohorts, which affects the direct comparison of bleeding rates between various populations and presenting conditions. A large portion of bleeding in this cohort was labeled as unspecified, which may affect accuracy of comparing bleeding sites between subgroups. In addition, this analysis does not include patients with nonprimary AHF diagnoses

and may not be generalizable to the larger population of patients with pre-existing HF who were hospitalized for other primary indications. The co-morbidities and associated conditions were coded based on the discharge diagnoses, and the temporal relation between the co-morbidities/procedures and bleeding during the hospitalization cannot be accurately determined. Data regarding the management of bleeding are not available in this dataset.

In conclusion, major bleeding occurs in 5.3% of patients hospitalized with AHF and occurs more commonly in patients with HFpEF than in patients with HFrEF and more commonly in men than in women. The common etiologies of bleeding include gastrointestinal, respiratory, hematuria, and procedural bleeding. The independent predictors of major bleeding include common cardiac and noncardiac co-morbidities, such as AMI, cardiogenic shock, and invasive procedures. Major bleeding is associated with higher inpatient mortality, LOS, and inpatient costs. These results have important clinical implications for the care of patients admitted with AHF by highlighting the risk factors and outcomes associated with significant bleeding.

Disclosures

The authors have no conflicts of interest to declare.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2022.12.017.

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