Research Article

Effect of Heart Failure With Preserved Ejection Fraction on Perioperative Outcomes in Patients Undergoing Hip Fracture Surgery

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Abstract

Introduction: Heart failure is a leading cause of morbidity and mortality in hip fracture surgery. The impact of heart failure with preserved ejection fraction (HFpEF) is poorly understood in this population. We designed a study to evaluate national perioperative outcomes in hip fracture for patients with HFpEF.

Methods: Patients with hip fracture undergoing total hip arthroplasty, hemiarthroplasty, or open/closed reduction with internal and external fixation from January 2005 to December 2013 were identified using the Nationwide Inpatient Sample. Inpatient outcomes during the index hospitalization were compared between patients without heart failure and with HFpEF. Heart failure with reduced ejection fraction was included as a secondary comparator. Perioperative major adverse cardiovascular and cerebrovascular events (MACCEs), defined as in-hospital all-cause death, acute myocardial infarction, and in-hospital cardiac arrest or acute ischemic stroke, were evaluated.

Results: Among 2,020,712 hospitalizations for hip fracture surgery, perioperative MACCE occurred in 67,554 hospitalizations (3.3%), corresponding to an annual incidence of approximately 7,506 events after applying sample weights. Compared with patients without heart failure, patients with HFpEF experienced increased odds of MACCE, adjusted odds ratio [aOR], 1.69; 95% confidence interval (CI), 1.51 to 1.89. In comparison, the aOR of experiencing a MACCE event in the heart failure with reduced ejection fraction group was 1.75 (95% CI, 1.57 to 1.96). HFpEF was also associated with increased odds of acute respiratory failure (aOR, 1.71; 95% CI, 1.53 to 1.91) and acute renal failure (aOR, 1.52; 95% CI, 1.41 to 1.64).

Conclusion: HFpEF confers a significant perioperative risk of MACCE in patients undergoing hip fracture surgery.

Hip fracture is a rapidly growing injury worldwide. Its global yearly incidence is expected to exceed 6 million by 2050[1] and is largely concentrated in the developed world where the elderly population is growing at unsurpassed rates. In the United States alone, the projected yearly incidence by 2040 is 510,000.[2] Major adverse cardiovascular and cerebrovascular events (MACCEs) are a leading source of perioperative morbidity and mortality,[3-6] resulting in prolonged hospitalization and increased resource utilization in hospitals. Heart failure is one risk

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factor most strongly associated with MACCE, both in the short- and long-term.[7,8]

Heart failure with reduced ejection fraction (HFrEF), or systolic heart failure, is the prototypical heart failure syndrome. The syndrome of heart failure with preserved ejection fraction (HFpEF), known also as diastolic heart failure, or diastolic dysfunction, is less understood. It has previously been categorized as a less severe perioperative risk factor than HFrEF, possibly comparable to the non-heart failure baseline in the perioperative window.[9,10] Current American College of Cardiology and American Heart Association (ACC/AHA) guidelines on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery state that there are limited data on perioperative risk stratification related to diastolic dysfunction.[11] In light of growing evidence of risk in noncardiac surgery,[12] and the pro-inflammatory milieu of acute hip fracture,[13-15] we hypothesize that patients with HFpEF are at notable risk of perioperative MACCE compared with patients without heart failure. Therefore, we conducted this study to quantify the risk of MACCE and secondary heart failure-related endpoints in HFpEF compared with the non-heart failure population, with HFrEF as a secondary comparator.

Methods

Data Source

Data were obtained from the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project-Nationwide Inpatient Sample (NIS) files yearly from 2005 through 2013. The NIS is the largest publicly available all-payer inpatient healthcare database in the United States. It provides data on 7 to 8 million hospital stays each year.[16] The NIS contains de-identified clinical and resource utilization information. Results from the NIS have been shown to correlate well with other national databases in the United States.[17] Approval for the use of the NIS patient-level data in this study was obtained from the Institutional Review Board and from the Healthcare Cost and Utilization Project.

Study Population

We used the *International Classification of Diseases, Ninth Edition, Clinical Modification* (*ICD-9-CM*) codes to identify patients aged 50 years or older, hospitalized for hip fracture surgery between January 2005 and December 2013, including open/closed reduction and internal fixation (RIF), hemiarthroplasty (Hemi), and total hip arthroplasty (THA) (Table 1, Supplemental Digital Content, http://links.lww.com/JAAOS/A357). Consistent with methodology used in previous studies to identify patients with heart failure, patients with HFpEF were identified using *ICD-9-CM* code 428.32 and HFrEF, using *ICD-9-CM* code 428.22.[18] Patients were excluded from the study if there were missing data on survival outcome upon discharge or were transferred in from another acute care hospital.

Definition of Variables

We used NIS variables to identify patients' age, sex, race, and day of admission (weekend or weekday) as well as hospital-level characteristics such as hospital region, size, location, and teaching status. Fracture characteristics and clinically relevant comorbidities were identified using the NIS Clinical Classification Software or using *ICD-9-CM* codes (Table 1, Supplemental Digital Content, http://links.lww.com/JAAOS/A357). Fractures were classified as transcervical, peritrochanteric, or unspecified/pathologic. The burden of comorbidities was assessed using the Charlson Comorbidity Score, which is based on 17 diagnosis categories with higher scores associated with higher in-hospital mortality.[19]

Study Outcomes

The primary outcome in this study was MACCE, a composite outcome measure consisting of the following in-hospital adverse events: mortality, acute myocardial infarction (AMI), cardiac arrest, or acute ischemic stroke. Secondary outcomes included acute respiratory failure, acute renal failure, and acute thromboembolic event. All corresponding *ICD-9-CM* codes are listed in Table 1 (Supplemental Digital Content, http://links.lww.com/JAAOS/A357).

Statistical Analysis

Weighting of patient-level observations was implemented to obtain national estimates for hospitalized hip fracture patients undergoing surgical repair. Patient- and hospital-level characteristics were compared between patients without heart failure and patients with HFpEF or HFrEF using the Pearson $\chi 2$ test for categorical variables and univariate linear regression (one-way analysis of variance) for continuous variables.

Odds ratios with 95% confidence intervals (CIs) were calculated by logistic regression analyses to examine the association of HFpEF or HFrEF with MACCE for all hip fracture patients undergoing surgery. Analysis models were adjusted for age, sex, race/ethnicity, fracture characteristics, surgical repair modality, obesity, tobacco use, hypertension, hyperlipidemia, diabetes mellitus, chronic kidney disease, end-stage renal disease on hemodialysis, coronary artery disease, previous revascularization with either percutaneous coronary intervention or coronary artery bypass surgery, peripheral arterial disease, previous venous thromboembolism, chronic lung disease, malignancy, weekend admission, hospital characteristics (region, size, and teaching status), and year of hospitalization. These variables were selected a priori based on factors used in the perioperative literature of hip fracture and replacement.[20-24] Several subgroup analyses were performed to validate the study findings. The incidence of perioperative MACCE was determined for each of the surgical repair modalities and stratified by heart failure subtype. To confirm established associations between the heart failure subtypes and perioperative risk for MACCE in this national data set, odds ratios with 95% CIs were calculated using multivariable logistic regression models for each of the surgical repair modalities: open/closed RIF, Hemi, and THA. These subgroup regression models were adjusted similar to those for the entire study population.

To examine the association of HFpEF or HFrEF with the secondary outcomes of acute respiratory failure, acute renal failure, and acute thromboembolic events, multivariable logistic regression models were constructed adjusting for age, sex, race/ethnicity, Charlson Comorbidity Index, fracture characteristics, surgical repair modality, median household income of the patient's ZIP Code of residence, primary payer, hospital characteristics (region, size, and teaching status), and year of hospitalization. Comorbidities of patients undergoing surgical repair are described in Table 2 (Supplemental Digital Content, http://links.lww.com/JAAOS/A357). Analyses were performed using Stata/MP version 13.0 (StataCorp, College Station, TX). All *P*-values were two sided with a significance threshold of $P < 0.05$.

Results

Study Population

Between January 2005 and December 2013, there were 2,020,712 hospitalizations for acute hip fracture surgery in patients aged 50 years and older. Among these, 31,118 (1.53%) were identified with HFpEF and 22,267 (1.10%) with HFrEF. Compared with patients without heart failure, patients with HFpEF and HFrEF were more likely to be older (79.5 years versus 83.7 and 82.0, respectively), non-Hispanic white (73.9% versus 80.3% and 80.6%), and have a higher burden of comorbidities (Table 1). Patients with HFpEF were more likely to be female (73.7% versus 72.5%), whereas patients with HFrEF were less likely to be females (54.2% versus 72.5%). Compared with patients without heart failure, those with HFpEF and HFrEF were less likely to be offered THA (3.8% versus 2.3% and 2.4%, respectively).

Major Adverse Cardiovascular and Cerebrovascular Events

Overall, MACCEs occurred in 67,544 of admissions for hip fracture that subsequently underwent surgery (3,340 events per 100,000 surgeries [3.34%]). In patients with HFpEF, MACCE occurred in 2,430 of 31,118 surgeries (7,810 events per 100,000 [7.81%]), whereas in patients with HFrEF, MACCE occurred in 1,944 of 22,267 surgeries (8,730 events per 100,000 [8.73%]). Compared with patients without heart failure, patients with HFpEF had an increased risk of perioperative MACCE after multivariable adjustment, adjusted odds ratio [aOR], 1.69 [95% CI, 1.51 to 1.89]. Patients with HFrEF had a comparable increased risk of perioperative MACCE, aOR, 1.75 [95% CI, 1.57 to 1.96]. Compared with patients without heart failure, patients with HFpEF had a statistically significant increased risk of AMI, aOR, 1.61 [95% CI, 1.37 to 1.90]; acute ischemic stroke, aOR, 1.51 [95% CI, 1.19 to 1.92]; cardiac arrest, aOR, 2.26 [95% CI, 1.66 to 3.07]; and death, aOR, 1.83 [95% CI, 1.56 to 2.15]. Perioperative risk for AMI, stroke, cardiac arrest, and death was comparable and similarly elevated in HFrEF patients (Table 2).

Surgery-specific Perioperative Risks

HFpEF and HFrEF patients undergoing open/closed RIF had similar perioperative risk of MACCE (7.3% versus 8.0%), AMI (3.1% versus 4.0%), acute ischemic stroke (1.2% versus 1.0%), cardiac arrest (0.7% versus 0.9%), and death (3.4% versus 4.0%). Perioperative risk for MACCE and its components was also comparable in HFpEF and HFrEF patients undergoing Hemi but not in those undergoing THA (Figure. 1). In the RIF group, HFpEF was associated with increased risk for development of MACCE, [aOR], 1.66 [95% CI, 1.45 to 1.90], similar to that of HFrEF, [aOR], 1.70 [95% CI, 1.47 to 1.98]. In the Hemi subgroup, HFpEF and HFrEF were similarly associated with an increased risk of developing MACCE, [aOR], 1.75 [95% CI, 1.45 to 2.10] and 1.80 [95% CI, 1.49 to 2.17], respectively. In the THA group, HFrEF was associated with an increased risk of MACCE, [aOR], 2.33 [95% CI, 1.15 to 4.70], whereas HFpEF was not, [aOR], 1.41 [95% CI, 0.64 to 3.09]. These relationships persisted for the MACCE components after multivariable adjustment except for acute ischemic stroke risk in patients undergoing RIF and cardiac arrest risk in patients undergoing THA. All surgery-specific findings are illustrated in more detail in Table 2.

Table 1

Baseline Characteristics of Patients Undergoing Surgical Repair for Hip Fracture With and Without Heart Failure

Characteristics	No. (%)			*P* Value HFpEF Versus No CHF	*P* Value HFrEF Versus No CHF
	Hip Fracture No HF (n = 1,967,327)	Hip Fracture HFpEF (n = 31,118)	Hip Fracture HFrEF (n = 22,267)		
Age, mean (SD), y	79.5 (10.3)	83.7 (8.0)	82.0 (8.4)	<0.001	<0.001
Female	1,426,586 (72.5)	22,939 (73.7)	12,059 (54.2)	0.040	<0.001
Race/ethnicity				<0.001	<0.001
White non-Hispanic	1,454,718 (73.9)	24,984 (80.3)	17,955 (80.6)		
Black non-Hispanic	62,513 (3.2)	1,239 (4.0)	924 (4.2)		
Hispanic	81,046 (4.1)	1,095 (3.5)	739 (3.3)		
Other race[a]	67,602 (3.5)	856 (2.7)	617 (2.8)		
Unknown	301,448 (15.3)	2,944 (9.5)	2,032 (9.1)		
Admission on weekend	528,304 (26.8)	8,181 (26.3)	6,220 (27.9)	0.310	0.097
Charlson comorbidity index					
0	891,892 (45.3)	—	—		
1	568,275 (28.9)	7,195 (23.1)	4,451 (20.0)		
≥2	507,160 (25.8)	23,923 (76.9)	17,816 (80.0)		
Type of fracture				<0.001	<0.001
Transcervical	509,715 (25.9)	7,079 (22.8)	5,210 (23.4)		
Peritrochanteric	954,035 (48.5)	16,780 (53.9)	11,521 (51.7)		
Other[b]	503,577 (25.6)	7,259 (23.3)	5,536 (24.9)		
Type of surgical repair				<0.001	<0.001
Reduction (open/closed) and internal fixation	1,236,845 (62.9)	20,195 (64.9)	14,138 (63.5)		
Hemi	655,567 (33.3)	10,219 (32.8)	7,593 (34.1)		
THA	74,915 (3.8)	704 (2.3)	536 (2.4)		

CHF = congestive heart failure, Hemi = hemiarthroplasty, HF = heart failure, HFpEF = heart failure with preserved ejection fraction, HFrEF = heart failure with reduced ejection fraction, THA = total hip arthroplasty
[a] Includes Asian/Pacific Islander and Native American race.
[b] Includes unspecified and pathologic hip fractures.

Secondary Outcomes

Patients with HFpEF had an increased risk of developing acute respiratory failure, aOR, 1.71 [95% CI, 1.53 to 1.91]. This risk surpassed that of patients with HFrEF, who had a smaller, but markedly elevated risk of developing acute respiratory failure when compared with patients without heart failure, aOR, 1.33 [95% CI, 1.16 to 1.51].

The risk of developing acute renal failure was similarly elevated in HFpEF and HFrEF. Compared with patients without heart failure, patients with HFpEF had an increased risk of developing acute renal failure, aOR, 1.52 [95% CI, 1.41 to 1.64]. Patients with HFrEF had a similarly increased risk, aOR, 1.46 [1.35 to 1.59]. The odds ratio of developing renal failure was slightly larger for patients with HFpEF than patients with HFrEF. The risk of developing acute thromboembolic events was similar among all groups. These findings are summarized in Table 3 (Supplemental Digital Content, http://links.lww.com/JAAOS/A357).

Discussion

In this multiyear analysis of over two million hospitalizations for hip fracture surgery, patients with HFpEF had an increased risk of perioperative MACCE when compared with patients without heart failure. This effect persisted in all of the MACCE subdomains of AMI, stroke, cardiac arrest, and in-hospital mortality. Patients with HFpEF were also at increased risk of developing acute respiratory and renal failure. These results illustrate

Table 2

Adjusted Odds of Perioperative Major Adverse Cardiovascular and Cerebrovascular Events by Type of Surgery and Heart Failure Status

Patient Group	Adjusted OR (95% CI)[a]									
	MACCE (Death/MI/ Stroke/IHCA)		Myocardial Infarction		Stroke		In-hospital arrest		Death	
	Adjusted	*P* Value	Adjusted	*P* Value	Adjusted	*P* Value	Adjusted	*P* Value	Adjusted	*P* Value
Overall[b]										
HFpEF	1.69 (1.51-1.89)	<0.001	1.61 (1.37-1.90)	<0.001	1.51 (1.19-1.92)	0.001	2.26 (1.66-3.07)	<0.001	1.83 (1.56-2.15)	<0.001
HFrEF	1.75 (1.57-1.96)	<0.001	1.83 (1.56-2.14)	<0.001	1.50 (1.14-1.97)	0.004	2.01 (1.41-2.86)	<0.001	1.89 (1.60-2.24)	<0.001
Reduction (open/ closed) and internal fixation[c]										
HFpEF	1.66 (1.45-1.90)	<0.001	1.51 (1.23-1.85)	<0.001	1.54 (1.13-2.09)	0.006	2.09 (1.40-3.12)	<0.001	1.82 (1.50-2.21)	<0.001
HFrEF	1.70 (1.47-1.98)	<0.001	1.74 (1.41-2.15)	<0.001	1.36 (0.94-1.98)	0.105	2.25 (1.45-3.50)	<0.001	2.00 (1.62-2.47)	<0.001
Hemi[c]										
HFpEF	1.75 (1.45-2.10)	<0.001	1.82 (1.43-2.32)	<0.001	1.52 (1.02-2.27)	0.042	2.31 (1.42-3.75)	0.001	1.84 (1.42-2.39)	<0.001
HFrEF	1.80 (1.49-2.17)	<0.001	1.98 (1.53-2.57)	<0.001	1.69 (1.10-2.58)	0.016	1.46 (0.76-2.80)	0.251	1.67 (1.26-2.21)	<0.001
THA[c]										
HFpEF	1.41 (0.64-3.09)	0.388	1.20 (0.39-3.68)	0.754	0.69 (0.08-5.88)	0.736	6.20 (1.39-27.61)	0.017	1.87 (0.66-5.26)	0.236
HFrEF	2.33 (1.15-4.70)	0.018	1.75 (0.65-4.70)	0.267	1.91 (0.38-9.65)	0.435	6.55 (1.25-34.37)	0.026	2.58 (0.97-6.83)	0.056

CI = confidence interval, Hemi = hemiarthroplasty, HFpEF = heart failure with preserved ejection fraction, HFrEF = heart failure with reduced ejection fraction, IHCA = in-hospital cardiac arrest, MACCE = major adverse cardiovascular and cerebrovascular events, MI = myocardial infarction, OR = odds ratio, THA = total hip arthroplasty

[a] Multivariable models include age, sex, race/ethnicity, obesity, tobacco use, hypertension, hyperlipidemia, diabetes mellitus, chronic kidney disease, end-stage renal disease on hemodialysis, coronary artery disease, previous revascularization with either percutaneous coronary intervention or coronary artery bypass surgery, peripheral arterial disease, previous venous thromboembolism, chronic lung disease, malignancy, weekend admission, hospital characteristics, and year of hospitalization as covariates. Reference is the population without heart failure.

[b] Overall models were additionally adjusted for type of fracture and surgical repair method.

[c] Type of surgery models were additionally adjusted for type of fracture.

HFpEF as a major perioperative risk factor and add to the complexity of the landscape of accelerated medical optimization in hip fracture surgery.

Our findings are consistent with the literature studying the impact of HFpEF in the nonorthopaedic perioperative window. A meta-analysis of 13 studies by Fayad et al[12] in 2016 found that patients with HFpEF undergoing noncardiac surgery were at increased risk of MACCE, myocardial infarction, and pulmonary edema. Our analysis expands the validity of these data to the previously unstudied hip fracture population and draws notable parallels between the perioperative deleterious effect of diastolic heart failure to that of systolic heart failure, where studies have shown that HFrEF patients are at increased risk of prolonged hospitalization, myocardial infarction, and death when undergoing hip fracture repair.[25-28]

Our subgroup analysis by surgical repair lends internal validity to these results because there is an anticipated increased risk of morbidity when comparing Hemi with RIF due to increased surgical time, increased surgical exposure, and blood loss. Increased risk of perioperative complications after Hemi as compared with RIF was consistent both in patients with HFpEF and HFrEF. In our study, 2.3% and 2.4% of patients with HFpEF and HFrEF, respectively, were treated with THA, as compared with 3.8% of patients without heart failure. The low incidence of THA in all groups renders conclusions about the relative risk profile of this surgery in patients with heart failure difficult to determine.

Our findings of increased odds of MACCE in HFpEF patients, treated with RIF or Hemi, are especially relevant due to the growing need to expeditiously optimize patients for hip repair. Management of hip fracture is uniquely centered around expedited time to surgery. Current organizational guidelines stress the importance of surgery within 48 hours, and evidence continues to favor quicker times to surgery as paramount to reducing risk of thromboembolic events, MACCE, and death.[29-31] Current trials studying the benefits of hyperaccelerated time to surgery to realize the benefits of ever-faster medical optimization are underway.[32] Because of the unique need to expedite medical optimization, we feel it is critical to understand and stratify the risk of various perioperative comorbidities. Currently, only two hard stop conditions exist in which the benefit of delaying surgery is felt to outweigh

Figure 1

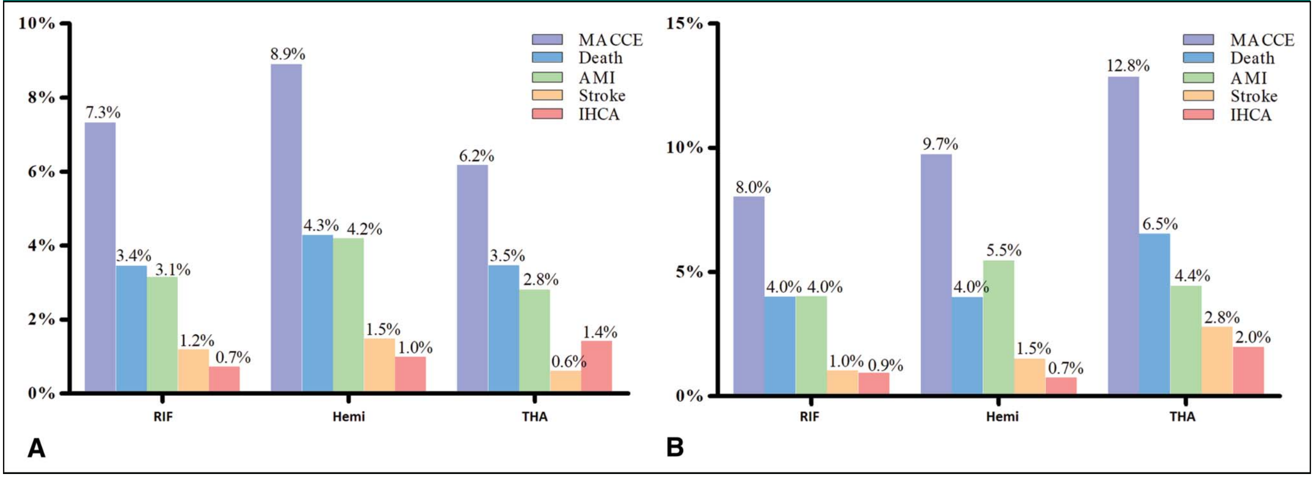

Chart showing primary outcomes in patients with (**A**) HFpEF and (**B**) HFrEF undergoing hip fracture surgery. AMI = acute myocardial infarction, HFpEF = heart failure with preserved ejection fraction, HFrEF = heart failure with reduced ejection fraction, Hemi = hemiarthroplasty, IHCA = in-hospital cardiac arrest, MACCE = major adverse cardiovascular and cerebrovascular event, RIF = open or closed reduction and internal fixation, THA = total hip arthroplasty

the risks: acute coronary syndrome and decompensated heart failure. Although coronary syndrome is well-defined, the degree, type, and severity of heart failure needed to reasonably delay surgery are nebulous.

Acute decompensated heart failure is associated with increased perioperative mortality, respiratory failure, and MACCE.[7,25,33] As such, aggressive optimization is preferred, even at the cost of delaying surgery. In practice, however, only systolic heart failure is treated so cautiously. The management of HFpEF has been historically met with clinical indecision, often as less severe than systolic heart failure.[10] Thus far, no consensus exists on optimal management of HFpEF, leading to heterogeneity in perioperative management. Considering the strong association between HFpEF and perioperative complications, we recommend heightened attention to this comorbidity during preoperative informed consent conversations and aggressive optimization of volume status perioperatively. The strong association between HFpEF and perioperative complications occurred both in patients undergoing RIF and Hemi. Although RIF may at times be considered a lower risk surgery, the data suggest that equal care should be taken in counseling patients regarding their risk of perioperative complications, whether planning for RIF or Hemi.

Our study adds to the existing literature by identifying HFpEF as a risk factor for perioperative MACCE[34-36] and heart failure decompensation in patients treated with surgery for hip fracture.[34,37,38] In our study, the risk profile of patients with HFpEF appeared more similar to those with systolic heart failure than to those without heart failure. Of interest, although HFpEF has been proposed as a less severe driver of volume overload compared with systolic heart failure,[10] patients with HFpEF were more likely to suffer respiratory failure than patients without heart failure and possibly even those with systolic heart failure. This suggests that clinicians underestimate the clinical significance of HFpEF, volume resuscitate too liberally, or both because data in other noncardiac surgeries support the increased incidence of pulmonary edema in patients with HFpEF.[34,37,38] These findings warrant increased scrutiny to the significance of HFpEF as a driver of adverse outcomes in the surgical patient and elevate the discussion of accelerated medical optimization in hip fracture, drawing parallels to systolic heart failure in the perioperative window.

Several limitations of this study should be considered. Our analysis is based on administrative and coding data collected through the NIS, which uses *ICD-9* coding data and is unable to ascertain the degree or severity of diagnoses or complications. For this reason, we selected hard endpoints free from notable diagnostic interpretation: the primary outcome was in-hospital MI, stroke, death, or cardiac arrest. Second, because of the nature of administrative databases, the timing of myocardial infarction or acute stroke could not be verifiably proven as occurring postoperatively. However, hip fracture surgery is absolutely contraindicated immediately after stroke or AMI, and as such it is highly likely that these outcomes developed postoperatively. Finally, the NIS database does not collect information after hospital discharge, and as such our analysis centers on complications that occurred during the index hospitalization.

Conclusions

We provide the largest presently available analysis of HFpEF as a risk factor in hip fracture surgery and have demonstrated increased MACCE, respiratory failure, and renal failure compared with patients without heart failure. Furthermore, patients with HFpEF undergoing both RIF and Hemi were found to be at increased risk for MACCE during the perioperative period. Our analysis demonstrates that HFpEF cannot be overlooked as a clinically insignificant comorbidity and that it portends the same potential for adverse outcomes traditionally associated with HFrEF. Our study adds nuance to the conversation about accelerated medical optimization before hip fracture surgery because the benefits of medical optimization must be weighed against the risks of surgical delay. We propose further trials assessing the outcomes associated with HFpEF in comparison to HFrEF in hip fracture treated with different surgeries for further granularity to the impact of each disease on patients before specific surgical interventions. We also suspect that future ACC/AHA guidelines in perioperative management will reflect the growing clinical entity of HFpEF and its associated risk.

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