

Predictability of Inpatient Mortality of Different Comorbidities in Both Types of Acute Decompensated Heart Failure: Analysis of National Inpatient Sample

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Abstract

Background: Several prediction models have been proposed to assess the short outcomes and in-hospital mortality among patients with heart failure (HF). Several variables were used in common among those models. We sought to focus on other, yet important risk factors that can predict outcomes. We also sought to stratify patients based on ejection fraction, matching both groups with different risk factors.

Methods: We conducted a retrospective cohort study utilizing the Healthcare Cost and Utilization Project National Inpatient Sample (HCUP-NIS) 2016 database.

Results: There were totally 116,189 admissions for acute decompensated heart failure (ADHF). Of these, 50.9% were for heart failure with reduced ejection fraction (HFrEF) group (n = 59,195), and 49.1% were for heart failure with preserved ejection fraction (HFpEF) group (n = 56,994). Overall, in-hospital mortality was 2.5% of admissions for ADHF (n = 2,869). When stratified by HF types, admissions for HFrEF had higher mortality rate (2.7%, n = 1,594) in comparison to admissions for HFpEF (2.2%, n = 1,275) (P < 0.001). Significantly associated variables in univariate analyses were age, race, hypertension, diabetes mellitus, chronic kidney disease (CKD), atrial fibrillation/flutter, obesity, and chronic ischemic heart disease (IHD), while

gender and chronic obstructive pulmonary disease (COPD) did not achieve statistical significance (P > 0.1).

Conclusions: To our knowledge, this is the first study to stratify HF patients based on ejection fraction and utilizing different predictors and in-hospital mortality. These and other data support the need for future research to utilize these predictors to create more accurate models in the future.

Keywords: Heart failure; In-hospital mortality; Ejection fraction; HFrEF; HFpEF

Introduction

Heart failure (HF) is a complex clinical syndrome that typically presents with either fluid overload or exercise intolerance. It can be caused by impaired left ventricle (LV) filling, impaired ejection of blood, or coexistence of both mechanisms. Ejection fraction (EF) has become the main determinant to differentiate between two major types of HF, heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF). It was estimated that 5.7 million Americans suffer from HF with projected increase in prevalence to exceed 8 million patients by 2030. Therefore, it remains a major direct and indirect cause of morbidity, mortality, and medical costs [1, 2].

Several prediction models were developed to predict the short-term outcomes of HF. In addition to providing prognostic information, such models can play a crucial role in the management of certain patients, especially when outcomes are predicted to be poor and early palliative consult and/or hospice referral become more reasonable. Most of those prediction models shared similar variables, renal function, age, and blood pressure being the most studied variables [3]. However, these modules have been underutilized in the daily clinical practice due to their limited accuracy in predicting serious events [4]. In addition to their limited ability to include all potential comorbidities, these models did not take into consideration the different types of HF. We sought to investigate the predictability of commonly associated comorbidities with in-hospital mortality among HF cohort. In addition to investigate whether the predictability, if any exist, is different between the two

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major types of HF, to be one step closer towards producing a model with better predictability.

Materials and Methods

Strobe guidelines were sought for reporting this manuscript [5].

Study design/settings

We conducted a retrospective cohort study utilizing the Healthcare Cost and Utilization Project National Inpatient Sample (HCUP-NIS) 2016 database. The database included a stratified sample of 20% of all-payer inpatient encounters in the USA. The encounters included in this database were systematically selected by the Agency for Healthcare Resources and Quality (AHRQ) to be representative of all the hospitalizations on the national level. The reported variables in this database include demographic variables, primary and secondary admission diagnoses, procedures, disposition, length of stay, and inpatient mortality, among others.

Participants

Encounters included in this study were hospitalizations for patients who were admitted primarily for acute HF, both systolic and diastolic. Patients with age < 18 year were excluded from the study. In addition, patient who have combined systolic and diastolic dysfunction were excluded to facilitate a direct comparison.

Variables

We sought to investigate demographic variables (age, sex, and race), and associated comorbidities/conditions (hypertension, chronic ischemic heart disease (IHD), diabetes mellitus, atrial fibrillation/flutter, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), obesity, hypertensive crisis, cardiogenic shock, acute coronary syndrome, pneumonias excluding influenza, and influenza). Primary outcome sought was inpatient mortality.

Data measurement

Clinical conditions, including acute decompensated heart failure (ADHF) (and its types) and concurrent comorbidities/conditions, were identified through their international classification of diseases, 10th revision (ICD-10 codes) that were recorded in the discharge record for each hospitalization.

Ethical considerations

No institutional review board (IRB) approval was obtained as

the data, on the national level, are completely de-identified. The study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

Statistical methods

Kolmogorov-Smirnov test was used to examine normality of continuous variables. Non-parametric continuous and categorical variables were described as median with interquartile range and frequencies, as appropriate. Chi-square test was used to compare categorical variables, and Mann-Whitney U test was used to compare non-parametric continuous variables. Variables associated with outcome in univariate analysis (P value < 0.10) were included in a logistic regression model (enter) to determine predictors of mortality. All analyses were done using IBM SPSS Statistics™ version 26.0 (IBM Corporation, Armonk, NY). An alpha value (P) of 0.01 was used to ascertain statistical significance given the large sample size.

Results

There were a total of 116,189 admissions for ADHF. Of these, 50.9% were admissions for HF_rEF group (n = 59,195) and 49.1% were for HF_pEF group (n = 56,994).

Missing data

Age, death during hospitalization, and gender had negligible missing values (0.0% (n = 6), 0.0% (n = 88), 0.0% (n = 39), respectively), while race was missing 3.35% (n = 3,768) of the data. Missingness of race data statistically correlated to age, discharge quarter, gender, and hospital division as well as other auxiliary variables (median household income for patient's zone improvement plan (ZIP) code and expected primary insurance) likely indicating data were missing not at random (MAR); however, imputation of missing data was not conducted as missing less than 5% of data are unlikely to introduce bias [6].

Baseline characteristics

Baseline characteristics are summarized in Table 1. Age distribution did not follow normal distribution. Median age was 74 years with a 25th - 75th interquartile range of 62 - 84 years. Female to male ratio was 1:1. White was the most prevalent race. Among the comorbidities explored in the study, hypertension was the most common.

Inpatient mortality

Overall, 2.5% of admissions for ADHF had death as outcome (n = 2,869). When stratified by HF types, admissions for

Table 1. Baseline Characteristics of Admitted Patients

	Median (interquartile range) or number (%)
Age (years)	74 (62 - 84)
Sex	
Male	58,525 (50.4)
Female	57,625 (49.6)
Race	
White	77,318 (66.5)
Black	21,313 (18.3)
Hispanic	8,521 (7.3)
Asian or Pacific Islander	2,233 (1.9)
Native American	498 (0.4)
Other	2,538 (2.2)
Comorbidities	
Hypertension	96,133 (82.7)
Chronic IHD	59,486 (51.2)
Diabetes mellitus	54,076 (46.5)
Atrial fibrillation/flutter	54,170 (46)
CKD	52,314 (45)
COPD	42,221 (36)
Obesity	27,359 (23.5)

IHD: ischemic heart diseases; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease.

HFrEF had higher mortality rate (2.7%, n = 1,594) than admissions for HFpEF (2.2%, n = 1,275) (P < 0.001).

Predictors of inpatient mortality

Inpatient mortality differed across different clinical characteristics (Table 2). Significantly associated variables in univariate analyses were age, race, hypertension, diabetes mellitus, CKD, atrial fibrillation/flutter, obesity, and chronic IHD; while gender and COPD did not achieve statistical significance (P > 0.1). Therefore, these factors were included in a multivariate logistic regression model, which showed that an increase of 10 years in age would increase the odds of inpatient mortality by 20%, and the presence of atrial fibrillation/flutter and CKD would increase the odds of inpatient mortality by 27% and 66%, respectively. While black race, hypertension, diabetes mellitus, and obesity would decrease the odds of inpatient mortality by 30%, 47%, 12%, 27%, respectively (Table 3).

Then, we stratified the data by EF. Variables statistically related in univariate analyses (P < 0.1) to inpatient mortality due to admissions for HFrEF were age, race, hypertension, diabetes mellitus, CKD, obesity, atrial fibrillation/flutter, and chronic IHD, but not gender or COPD. While variables associated with inpatient mortality of HFpEF, in univariate analyses, were age, race, hypertension, diabetes mellitus, atrial fibrillation/flutter, CKD, obesity, and COPD. Results of mul-

tivariable logistic regression models for each type are shown in Table 4. Notably, Black race specifically decreased odds of inpatient mortality of patients with HFrEF, but not with HFpEF, while diabetes mellitus specifically decreased odds of patients with HFpEF, not with HFrEF. Similarly, obesity and COPD independently predicted lower and higher inpatient mortality for patients with HFpEF, but not with HFrEF; while age, hypertension, atrial fibrillation/flutter, and CKD independently predicted inpatient mortality in both HFrEF and HFpEF.

Discussion

The American College of Cardiology Foundation/American Heart Association (ACCF/AHA) Task Force currently uses a cutoff of no more than 40% EF to define HFrEF and less than 50% to define HFpEF; while classification of EF of 41-49% depends on the clinical evaluation. If the clinical course resembles that of HFpEF, it is considered “HFpEF borderline”, and if EF was < 40%, but subsequently improved, it is classified as “HFpEF improved” [7, 8]. To date, the majority of the clinical trials and observational studies conducted on HF patients have focused on the HFrEF group. Therefore, the features of other types of HF are still poorly understood [7, 9].

Despite the fact that hypertension and diabetes are well-known risk factors for developing HF, our study showed a protective impact with no increase in the in-hospital mortality

Table 2. Correlations Between Inpatient Mortality and Different Clinical Characteristics

	Outcomes, frequency (%)		P value
	Died	Discharged alive	
Age (mean rank)	70,558.94	57,730.99	< 0.001
Gender			
Male	1,462 (2.5)	57,022 (97.5)	0.52
Female	1,406 (2.4)	56,172 (97.6)	
Race			
White	2,160 (2.8)	75,089 (97.2)	< 0.001
Black	300 (1.4)	20,997 (98.6)	
Hispanic	163 (1.9)	8,356 (98.1)	
Asian or Pacific Islander	67 (3)	2,166 (97)	
Native American	13 (2.6)	485 (97.4)	
Other	49 (1.9)	2,489 (98.1)	
Hypertension			
Yes	2,131 (2.2)	93,937 (97.8)	< 0.001
No	738 (3.7)	19,295 (96.3)	
Chronic IHD			
Yes	1,514 (2.5)	57,934 (97.5)	0.08
No	1,355 (2.4)	55,298 (97.6)	
Diabetes mellitus			
Yes	1,143 (2.1)	52,893 (97.9)	< 0.001
No	1,726 (2.8)	60,339 (97.2)	
Atrial fibrillation/flutter			
Yes	1,672 (3.1)	52,450 (96.9)	< 0.001
No	1,197 (1.9)	60,782 (98.1)	
CKD			
Yes	12,819 (5)	244,420 (95)	< 0.001
No	13,008 (4.1)	303,566(95.9)	
COPD			
Yes	1,068 (2.5)	41,123 (97.5)	< 0.32
No	1,801 (2.4)	72,109 (97.6)	
Obesity			
Yes	417 (1.5)	26,926 (98.5)	< 0.001
No	2,452 (2.8)	86,306 (97.2)	

IHD: ischemic heart diseases; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease.

among both HF groups. The mechanisms beyond these two findings remain yet to be understood. In theory, these factors can lead to chronic ischemia promoting the development of collateral circulation, which makes the myocardium less vulnerable to ischemic events and enhances myocardial perfusion [9, 10]. Furthermore, it was also debated that chronic IHD would indeed improve the long-term survival of patients with HF [11, 12]. However, we could not find any evidence on short-term outcomes, and our models have showed that chronic CHD fails to predict inpatient survival in patients with

ADHF, regardless of the type.

Our study has found obesity to be a protective factor and can predict survival among HFpEF cohort. Obesity is a well-known risk factor for cardiovascular diseases. Nevertheless, the concept of obesity paradox has gained popularity in the last few years. There is no doubt that visceral fat is a risk factor [13]. However, subcutaneous fat, in metabolically healthy patients, was associated with better outcomes in patients with established cardiovascular [14, 15]. The concept of obesity paradox extends to include outcomes of HF. While all stages

Table 3. Multivariate Logistic Regression Model to Predict Inpatient Mortality of Acute Decompensated Heart Failure

	N (admissions)	OR	99% CI for OR	P value
Age	116,183	1.022	1.017 - 1.027	< 0.001
Race				
White	77,318	1		Ref
Black	21,313	0.70	0.59 - 0.83	< 0.001
Hispanic	8,521	0.84	0.67 - 1.04	0.03
Asian or Pacific Islander	2,233	1.13	0.81 - 1.56	0.33
Native American	498	1.17	0.56 - 2.44	0.56
Other	2,538	0.79	0.54 - 1.16	0.12
Hypertension	96,133	0.53	0.47 - 0.60	< 0.001
Chronic IHD	59,486	0.99	0.90 - 1.10	0.97
Diabetes mellitus	54,076	0.88	0.79 - 0.98	0.003
Atrial fibrillation/flutter	54,170	1.27	1.14 - 1.41	< 0.001
CKD	52,314	1.66	1.50 - 1.85	< 0.001
Obesity	27,359	0.73	0.63 - 0.85	< 0.001

IHD: ischemic heart diseases; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; OR: odds ratio; CI: confidence interval.

of obesity remain a risk factor to develop HF, it seems to be associated with better outcomes in patients with established diagnosis of HF [16], and this effect seems to be applicable on the inpatient outcomes and long-term outcome alike. Further studies focusing on stratifying the obesity based on severity and adiposity might lead to establishing a clear association between the obesity and the outcome in the cardiovascular diseases.

Gender difference is one of the factors that have not been well studied in HF due to women underrepresentation in most of the HF clinical trials [17]. The impact of gender on the outcomes of HF is still controversial, with some studies detecting a difference favoring better outcome in women and other studies failing to detect any difference [18-20]. Based on our results, gender failed to predict inpatient mortality.

African Americans, followed by Hispanics, are more likely

Table 4. Multivariate Logistic Regression Model to Predict Inpatient Mortality of Acute Decompensated Heart Failure Types

	HF _r EF			HF _p EF		
	OR	99% CI for OR	P value	OR	99% CI for OR	P value
Age	1.02	1.01 - 1.02	< 0.001	1.03	1.02 - 1.03	< 0.001
Race						
White	1		Ref			Ref
Black	0.63	0.51 - 0.78	< 0.001	0.78	0.56 - 1.03	0.02
Hispanic	0.80	0.60 - 1.06	0.04	0.89	0.64 - 1.25	0.38
Asian or Pacific Islander	1.02	0.65 - 1.60	0.92	1.30	0.81 - 2.10	0.14
Native American	1.22	0.50 - 2.95	0.55	1.06	0.29 - 3.95	0.89
Other	0.71	0.43 - 1.17	0.08	0.91	0.51 - 1.63	0.70
Hypertension	0.56	0.48 - 0.66	< 0.001	0.51	0.42 - 0.61	< 0.001
Chronic IHD	0.98	0.85 - 1.13	0.69	Not included in the model		
Diabetes mellitus	0.93	0.81 - 1.08	0.22	0.84	0.71 - 0.99	0.006
Atrial fibrillation/flutter	1.25	1.09 - 1.44	< 0.001	1.29	1.10 - 1.51	< 0.001
CKD	1.75	1.51 - 2.01	< 0.001	1.57	1.35 - 1.83	< 0.001
Obesity	0.87	0.70 - 1.07	0.93	0.70	0.57 - 0.87	< 0.001
COPD	Not included in the model			1.241	1.06 - 1.44	< 0.001

HF_rEF: heart failure with reduced ejection fraction; HF_pEF: heart failure with preserved ejection fraction; IHD: ischemic heart diseases; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; OR: odds ratio; CI: confidence interval.

to develop HF which is likely attributed to a higher incidence of risk factors such as hypertension and diabetes mellitus in these ethnic groups [21]. Despite an increased prevalence, African Americans and Hispanics had significantly lower 30-day and 1-year mortality rates compared to whites in retrospective cohort studies [22]. Likewise, our results revealed whites had the highest mortality (2.8%) when compared to African Americans (1.4%) and Hispanics (1.9%). In our study, the decreased mortality in the Hispanic population when compared to whites was observed, and is in agreement with previous literature; however, did not achieve statistical significance. This phenomenon has been attributed to these ethnic groups seeking medical care in emergency departments over outpatient centers due to lack of resources, language barriers, or financial burden when compared to whites leading to more aggressive and early management, but an increased rate of inpatient readmissions [22-24].

The impact of concomitant COPD among patients with HF is very scant in the literature [25]. These two conditions often coexist. A multicenter prospective cohort study showed no differences in inpatient mortality between patients with coexistent COPD and HF and patients with HF alone [26]. However, mortality at 1 year was higher in patients with coexistent COPD, likely because they received less evidence-based care for HF, such as lack of beta blockers, due to the presumed contraindication in patients with COPD [26, 27]. Similarly, we found that COPD fails to predict inpatient mortality in patients with ADHF. However, when further stratified by HF types, COPD indeed predicted higher mortality among patients with ADHF due to HFpEF.

Around 30% of patients with HF have CKD. The association of these two conditions is bidirectional. The existence of the CKD frequently delays the diagnosis of HF; hence, it delays the initiation of evidence-based care subsequently. Most CKD patients die from cardiovascular complications, and the presence of HF makes the progression of the CKD faster, which emphasizes the bidirectional relationship [28, 29]. We found that CKD was an independent predictor of inpatient mortality, roughly increasing the risk by 1.75 times in HFrEF group and 1.5 times in HFpEF group. However, this does not necessitate that CKD is associated with higher risk of mortality among HFrEF group, as comparison between the two regression models is invalid, and pooling of data is, perhaps, needed for a direct comparison.

The coexistence of HF and atrial fibrillation has been established long time ago with estimated prevalence of 41% in HF population. Similarly, poor prognosis is established when both conditions coexist [30]. Several mechanisms have been put forward to explain the poorer outcome, such as loss of atrial contribution to the cardiac output, tachycardia induced cardiomyopathy, and atrial fibrosis which also leads to conduction abnormalities increasing the risk of developing atrial fibrillation [31-33]. We found that atrial fibrillation independently predicted inpatient mortality in both types of HF.

Our study has strengths and limitations. Strengths include the large sample size, the statistically conservative approach by setting alpha error cutoff of 0.01, and the selection of variables that only strongly predict inpatient mortality in a univariate analysis ($P < 0.1$) to be included in the multivariate

analyses. We also recognize several limitations including, but not limited to, that the utilized data is an administrative data created primarily for billing purposes. The diagnoses were determined by the relevant ICD-10 codes for each clinical condition, which can result in selection bias, depending on the accuracy of the codes abstractors. Last but not least, it was unknown for us whether the classification of HFrEF and HFpEF was indeed based on the criteria set by ACCF/AHA Task Force guidelines.

Conclusions

Our study sheds the light on the association between and the predictability of multiple comorbidities on the inpatient mortality of admissions for ADHF. We found differences between the predictability of these comorbidities between the two major types of HF, with or without reduced EF. Further studies using these comorbidities along with biochemical markers and implementation of the underlying type of HF might lead to creation of a more accurate prediction model of inpatient mortality.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Informed Consent

Not applicable.

Author Contributions

Abdulrahman Museedi: conceptualization, formal analysis, investigation, visualization, writing original draft, review, and editing. Abbas Alshami: conceptualization, formal analysis, investigation, visualization, writing original draft, review, and editing. Steven Douedi: investigation, visualization, writing original draft, review, and editing. Firas Ajam: investigation, visualization, writing original draft, review, and editing. Joseph Varon: supervision, visualization, writing review, and editing. All authors approve of the final version of this manuscript for publication.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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