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Impact and Outcomes of Patients with Congestive Heart Failure Complicating Non-ST-Segment Elevation Myocardial Infarction, Results from a Nationally-Representative United States Cohort

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ABSTRACT

Introduction: Congestive heart failure (CHF) is seen in up to 13–25% of patients with NSTEMI. Recent data describing the impact of congestive heart failure (CHF) on in-hospital outcomes in patients with non-ST-segment elevation myocardial infarction (NSTEMI) in the United States is limited. We sought to examine the in-hospital outcomes, and management of CHF in patients admitted to the hospital with NSTEMI.
Methods: National Inpatient Sample (NIS) database (2010–2014) was analyzed to identify patients with NSTEMI using ICD-9-CM codes. The primary outcome was in-hospital mortality. Propensity score-matching analysis compared mortality in CHF patients to matched controls without CHF.
Results: Of 247,624 patients with NSTEMI, 84,115 (34%) had CHF. Patients with CHF were less likely to receive percutaneous coronary intervention (PCI) [20.48% vs. 40.9%, $P < 0.001$] or coronary artery bypass grafting (CABG) [8.2% vs 9.6%, $P < 0.001$] during hospitalization. Also, they had longer lengths of stay and higher risk for in-hospital adverse outcomes. CHF was the strongest predictor of in-hospital death. The increased mortality risk was persistent after propensity matching (RR 1.27; 95% CI 1.22 to 1.33).
Conclusion: CHF among patients with NSTEMI is associated with increased risk for in-hospital mortality and adverse outcomes.

1. Introduction

In the United States (US), >625,000 patients annually experience non–ST-segment elevation myocardial infarction (NSTEMI) [1,2]. Congestive heart failure (CHF) is a frequently seen complication in patients with NSTEMI and approximately 13 to 25% of the patients with NSTEMI in the United States present with CHF or develop CHF during hospitalization [3,4]. Furthermore, several studies have described the presence of heart failure in patients hospitalized for NSTEMI as an independent predictor of treatment disparity and increased mortality and morbidity at 30-day follow-up [5–7]. During the past decade, considerable improvements in NSTEMI revascularization and noninvasive therapies have occurred, along with a remarkable increase in the prevalence of cardiovascular (CV) and non-CV comorbidities [8]. Nevertheless, contemporary data describing national in-hospital outcomes, impact and management of CHF complicating NSTEMI hospitalizations in the US population is limited. Previous studies have evaluated CHF among the full spectrum of acute coronary syndrome, but not specifically NSTEMI [9–14]. Earlier studies among the NSTEMI population have been limited to community-based settings or descriptions of events up to the early 2000s [3,7,14,15]. This study aims to update literature on the outcomes, and management, of CHF in patients hospitalized for NSTEMI using the 2010 through 2014 National Inpatient Sample (NIS) databases.

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Table 1
Baseline characteristics of patients and procedures performed according to presence of absence of congestive heart failure.

Characteristic	CHF (N = 84,115) (34%)	No CHF (N = 163,509) (66%)	P-value
Age, mean (SD)	73.3 (12.6)	66 (13.7)	<0.001
Female, N (%)	38,913 (46.26%)	63,637 (38.92%)	<0.001
Male, N (%)	45,202 (53.74%)	99,872 (61.08%)	<0.001
Deyo-Charlson Index, mean (SD)	4.4 (SD: 1.8)	2.3 (SD: 1.6)	<0.001
Hypertension, N (%)	69,533 (82.66%)	128,049 (78.31%)	<0.001
Diabetes, N (%)	42,528 (50.56%)	59,216 (36.22%)	<0.001
CKD, N (%)	35,480 (42.18%)	26,112 (15.97%)	<0.001
Ischemic stroke/TIA (%)	4700 (5.59%)	6220 (3.80%)	<0.001
Procedures			
PCI, N (%)	17,226 (20.48%)	66,873 (40.9%)	<0.001
CABG, N (%)	6894 (8.2%)	15,709 (9.6%)	<0.001

2. Material and methods

2.1. Data sources

The study reviewed data from the National Inpatient Sample (NIS) database which is part of the Healthcare Cost and Utilization Project (HCUP), sponsored by Agency for Healthcare Research and Quality [16]. NIS is the largest all-payer database of inpatient stays in the United States. Drawn from all hospitals participating in HCUP, it provides data from a 20% stratified sample of discharges from U.S. hospitals, excluding rehabilitation and long-term acute care hospitals [16]. Given the retrospective nature of this study, the Wayne State Institutional Review Board did not require informed consent for this study.

2.2. Study design

We identified patients with NSTEMI from 2010 to 2014 using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes 410.7x when listed as a primary diagnosis. The primary diagnosis is the condition chiefly responsible for hospitalization (after clinical evaluation and diagnostic investigation) and is usually derived after reviewing the patient admission record according to the AHRQ [17]. We divided the cohort into two groups based on the presence of CHF defined by the ICD codes (402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, and 428.x) when listed as a secondary diagnosis. These ICD-9-CM codes have been validated and also used in previous studies examining the NIS to identify patients with CHF [18–21]. Patients <18 years were excluded. Also, patients with cardiogenic shock or missing data on age, length of stay, gender, primary diagnosis and death were excluded. We also excluded patients who were admitted electively or transferred to another acute hospital. The primary outcome was in-hospital mortality in patients with CHF compared to the no-CHF group. Secondary outcomes included; ventricular tachycardia (VT), respiratory failure requiring mechanical ventilation and acute kidney injury (AKI). We examined the length of hospital stay (LOS), and hospital stay >3 (median) was considered prolonged. The study compared baseline characteristics including demographic data (age and gender), relevant cardiovascular risk factors and clinical co-morbidities. Secondary diagnoses, comorbidities, and procedures performed during hospitalization were identified using the ICD-9-CM codes (Supplemental Table 6). We calculated the Deyo-Charlson comorbidity index for all study subjects. The Deyo-Charlson comorbidity index is a tool to estimate the severity of co-morbid condition [22]. Its use to predict mortality in administrative databases has been previously validated [23]. The index incorporates 17 comorbid conditions including CHF, diabetes mellitus (DM) with and without complications, MI, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), stroke and intracranial bleed, dementia, mild and severe liver disease, acquired immune deficiency syndrome (AIDS), cancer with and without metastatic disease, peripheral vascular disease and rheumatic diseases [22].

2.3. Statistical analysis

Chi-square and student *t*-tests compared categorical and continuous variable respectively. Multivariable logistic regression compared the Adjusted Odds Ratios (AOR) for the outcome, accounting for baseline characteristics that showed a significant univariate difference in the two study groups. We subsequently calculated propensity scores for all study subjects using demographic and clinical variables that are associated with the development of CHF and the primary outcome. The final model included: age, gender, DM, HTN, CKD, use of percutaneous coronary intervention (PCI), Charlson Index, and ischemic stroke or TIA. We performed propensity matching with the 1:1 nearest neighbour algorithm [24]. To ensure that analysis achieved adequate balance in the baseline characteristic we calculated standardized differences between the two cohorts. Matching was considered successful when the standardized difference was <10% [25]. The study used STATA 14 (Stata Corp, College Station, Texas).

3. Results

Out of 247,624 patients with NSTEMI who met inclusion criteria, 84,115 (34%) presented with or developed CHF during admission. Baseline patient characteristics are summarized in Table 1. Patients with CHF were older (73.3 ± 2.6 vs. 66 ± 3.7 years, $P < 0.001$) and more likely to be female (46.26% vs. 38.92%, $P < 0.001$). Furthermore, patients with CHF were more likely to have diabetes, hypertension, chronic kidney disease and ischemic stroke or transient ischemic attacks (TIA). However, patients with CHF were less likely to receive percutaneous coronary intervention (PCI) [20.48% vs. 40.9%, $P < 0.001$] or coronary artery bypass grafting (CABG) [8.2% vs 9.61%, $P < 0.001$] during hospitalization (Table 1). Hospital outcomes are shown in Table 2. In-hospital mortality was three times higher for patients with CHF than those without CHF on admission or during hospitalization (5.02% vs. 1.64%; $P < 0.001$). Patients with CHF complicated NSTEMI experienced worse clinical outcomes including ventricular tachycardia (6.1% vs. 3.1%), respiratory failure requiring mechanical ventilation (5.67% vs. 2.04%), and acute kidney injury (26.3% vs. 9.0%) (all $P < 0.001$). Furthermore, CHF development was significantly associated with a longer hospital stay (hospital stay >3 days adjusted odds ratio [AOR] 2.3; 95% confidence interval (CI) 2.26 to 2.36, $P < 0.001$). Multivariate logistic regression analysis adjusted for potential confounding factors is shown in Table 3.

Table 2
Primary and secondary outcomes in patients with and without congestive heart failure.

Variable	With CHF	Without CHF	AOR	95% CI	P-value
In-patient mortality	4223 (5.02%)	2681 (1.64%)	1.57	(1.47–1.64)	<0.001
Ventricular tachycardia	5102 (6.1%)	5080 (3.1%)	2.16	(2.06–2.27)	<0.001
Mechanical ventilation	4769 (5.67%)	3332 (2.04%)	2.2	(2.09–2.32)	<0.001
Acute kidney injury	22,126 (26.3%)	14,706 (8.99%)	1.87	(1.82–1.93)	<0.001
Length of stay, days, median (IQR)[a]	4 (3–8)	3 (2–4)			<0.001
Hospital stay > 3 days	52,542 (62.46%)	53,592 (32.78%)	2.3	(2.26–2.36)	<0.001

[a] (IQR) interquartile range.

Table 3
Multivariate logistic regression analysis of predictors of hospital death.

Variable	AOR	95% CI
CHF	1.57	(1.47–1.64)
Stroke/TIA	1.27	(1.16–1.39)
Deyo-Charlson Index	1.18	(1.16–1.19)
Age (per year)	1.05	(1.04–1.10)
Diabetes	0.80	(0.76–0.85)
CABG	0.77	(0.70–0.85)
Hypertension	0.52	(0.49–0.55)
PCI	0.28	(0.26–0.30)

Table 4
Congestive heart failure impact on Inpatient Mortality after 1:1 Propensity matching.

Variable	CHF (N = 84,115)	NO CHF (N = 84,115)	% Standard bias
Age (mean in years)	73.328	73.412	−0.6
Female	46.26%	46.45%	−0.4
Diabetes	50.56%	50.87%	−0.6
Hypertension	82.66%	83.74%	−2.7
CKD	42.18%	41.69%	1.1
PCI	20.48%	20.53%	−0.1
CABG	8.20%	7.58%	2.2
Charlson Index (mean score)	4.442	4.4291	0.8
Ischemic stroke/TIA	5.59%	4.98%	2.9
In-patient mortality*	5.02%	3.94%	6

* In-patient mortality Relative Risk (RR) 1.27; 95% CI (95% 1.22–1.33); (P-value < 0.001).

Congestive heart failure on admission or during hospitalization was the strongest predictors of in-hospital death (AOR 1.57; 95% CI 1.47 to 1.64, P < 0.001). Other independent predictors of death include acute ischemic stroke or transient ischemic attack, high Deyo-Charlson comorbidity index, and older age. Propensity score-matched analysis result showed a statistically significant difference in the rate of in-hospital mortality between the two groups (5.2% vs. 3.94%, Relative Risk 1.27; 95% CI 1.22 to 1.33). However, the CHF-NSTEMI patients who underwent PCI had a lower mortality risk (AOR 0.38; 95% CI 0.33 to 0.42, P < 0.001) compared to the no-PCI group.

4. Discussion

Drawn from over 7 million hospital stays per year nationwide; our large study population was a representative sample of patients presenting with NSTEMI in the U.S. between 2010 and 2014 [16]. In this "real world" sample, 34% of patients with NSTEMI present with or develop CHF during admission. Patients with CHF in our study share a similar high-risk profile with patients in previous studies including older age and higher rates of co-morbidities including diabetes, hypertension, and chronic kidney disease [3,4,15]. Furthermore, CHF association with other in-hospital outcomes was concordant with the trend described by Roe et al. and Bahit et al. namely that patients with CHF either at presentation or during hospitalization experienced more adverse clinical outcomes and higher in-hospital mortality [3,4]. We may postulate that patients with CHF and NSTEMI have a predetermined high-risk profile, which puts them at risk of experiencing adverse clinical outcomes amid any new ischemic insult. However, in this study that background risk profile alone did not fully explain the adverse outcomes paradigm among the CHF patients. Propensity matching was used to establish matched cohorts to control for baseline differences between the two groups yet patients with CHF had statistically significant higher in-patient mortality when compared with patients with no CHF. The last finding illustrates that in patients with NSTEMI, CHF at any time during hospitalization is one of the most influential predictors of poor prognosis and high in-hospital mortality (Table 4).

The 2009 focused update incorporated into the American College of Cardiology Foundation/American Heart Association Task (ACC/AHA) 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults recommended early coronary catheterization with intent to perform revascularization in NSTEMI patients with heart failure (class IB indication) [26]. In our study similar to the previous studies, patients with NSTEMI who presented with or developed CHF during admission were less likely to undergo coronary revascularization (PCI or CABG) [4,15]. The increased frequency of CKD and the increased incidence of AKI observed among the NSTEMI-CHF patients may have driven the antecedent observation. Gupta et al. compared the PCI outcomes among patients with CKD, patients with end-stage renal disease (ESRD), and those with normal renal function [27]. Patients with renal insufficiency had higher in-hospital mortality, higher post-PCI hemorrhage, and higher cost of hospitalization [27]. Furthermore, there was a 14 fold increase in the risk of AKI requiring dialysis among the renal insufficiency patients [27]. However, other essential elements of the patient's history (e.g., electrocardiogram (ECG) monitoring details, prior stress tests results or previous coronary angiograms results) were beyond the data included in the patient sample [28]. The previously mentioned parameters are needed for the proper identification of the patients who will derive benefits from coronary revascularization [28]. Therefore, further studies are required in order to verify our results and to determine barriers to coronary revascularization in the NSTEMI-CHF subpopulation. Nevertheless, the NSTEMI-CHF patients who underwent PCI in our study had a lower mortality risk (AOR 0.38; 95% CI 0.33 to 0.42, P < 0.001) compared to the no reperfusion cohort (Table 5). The last findings are concordant with the findings of Audrey et al. whom also showed a statistically significant reduction in mortality in NSTEMI patients with CHF who underwent revascularization [9].

Surprisingly in our study patients having pre-existing diabetes or hypertension were at lower risk of inpatient mortality, this could be explained by the improved compliance with the guidelines directed therapy for both conditions over the last decade. Consequently, prior to arrival, these patients are usually on aspirin, angiotensin-converting enzyme inhibitors or angiotensin receptors blockers and other medications that have a proven mortality benefit for patients with NSTEMI and CHF. However, the NIS database does not capture variables related to the severity of HTN or DM such as hemoglobin A1c, insulin treatment, details of HTN complications, etc. Therefore, we were not able to exclude the possibility that the severity of DM and HTN was less in the CHF cohort.

This study one of the largest studies to examine the impact of CHF on inpatient mortality and outcomes in patients with NSTEMI. However, there are several limitations to our study. First, this is an observational study. Despite the use of propensity score analysis, there is the risk of unmeasured confounder in the analysis, the NIS database does not capture variables related to etiopathology, severity, and management of CHF such as ejection fraction, adherence to treatment with guidelines directed medical therapy, and details of the in-hospital complications. Therefore, the impact of the antecedent variables on outcomes cannot be determined, and our ability to precisely identify opportunities to

Table 5
Survival outcomes with and without percutaneous coronary intervention in the patients with congestive heart failure complicated non-ST-segment elevation myocardial infarction.

	No PCI (N = 66,889)	PCI (N = 17,226)	AOR	95% CI	P-value
In-patient mortality, %	3900 (5.8%)	323 (1.9%)	0.38	(0.33–0.42)	<0.001

reduce the adverse outcomes among the NSTEMI-CHF group are limited. Nevertheless, the analysis of large administrative databases is a useful resource for hypothesis-generation [29]. Second, we are uncertain whether CHF during hospitalization is new onset CHF or a consequence of a previous condition, but we aimed to examine the impact of CHF regardless of the onset. Third, the analysis of large administrative data carries the possibility of miscoding. Finally, the outcome data are limited to in-hospital events and long-term impact and outcomes could not be assessed. However, the NIS database is a reliable representative of the target U.S. hospitals population with broad applicability and has been used and validated in many previous studies [30].

5. Conclusion

CHF in patients with NSTEMI is associated with increased risk for in-hospital mortality and adverse outcomes. Despite their increased risk, CHF patients are less frequently treated with revascularization strategies. Further prospective studies to determine and overcome barriers to early revascularization in this high-risk group of patients are needed.

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Conflict of interest

None of the authors have any conflicts of interest to declare.

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