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Clinical Investigation

Hospitalized Patients with Heart Failure and Common Bacterial Infections: A Nationwide Analysis of Concomitant *Clostridium Difficile* Infection Rates and In-Hospital Mortality

PETRA MAMIC, MD,[1] PAUL A. HEIDENREICH, MD,MS,[1,2,3] HALEY HEDLIN, PhD,[1] LAKSHIKA TENNAKOON, MD,MS,[1] AND KRISTAN L. STAUDENMAYER, MD,MS[1]

Stanford and Palo Alto, California

ABSTRACT

Background: Patients with heart failure (HF) are frequently hospitalized with common bacterial infections. It is unknown whether they experience concomitant *Clostridium difficile* infection (CDI) more frequently than patients without HF, and whether CDI affects their mortality.

Methods: We used 2012 National Inpatient Sample data to determine the rate of CDI and associated in-hospital mortality for hospitalized patients with comorbid HF and urinary tract infection (UTI), pneumonia (PNA), or sepsis. Univariate and multivariate analyses were performed. Weighted data are presented.

Results: There were an estimated 5,851,582 patient hospitalizations with discharge diagnosis of UTI, PNA, or sepsis in 2012 in the United States. Of these, 23.4% had discharge diagnosis of HF. Patients with HF were on average older and had more comorbidities. CDI rates were higher in hospitalizations with discharge diagnosis of HF compared with those without HF (odds ratio 1.13, 95% confidence interval 1.10–1.16) after controlling for patient demographics and comorbidities and hospital characteristics. Among HF hospitalizations with UTI, PNA, or sepsis, those with concomitant CDI had a higher in-hospital mortality than those without concomitant CDI (odds ratio 1.81, 95% confidence interval 1.71–1.92) after controlling for the covariates outlined previously.

Conclusions: HF is associated with higher CDI rates among hospitalized patients with other common bacterial infections, even when adjusting for other known risk factors for CDI. Among these patients with comorbid HF, CDI is associated with markedly higher in-hospital mortality. These findings may suggest an opportunity to improve outcomes for hospitalized patients with HF and common bacterial infections, possibly through improved *Clostridium difficile* screening and prophylaxis protocols. (*J Cardiac Fail 2016;*■■:■■–■■)

Key Words: Heart failure, *Clostridium difficile*, hospitalization, outcomes.

From the [1]Department of Medicine, Stanford University School of Medicine, Stanford, California; [2]VA Palo Alto Health Care System, Palo Alto, California and [3]Stanford Cardiovascular Institute, Stanford, California.

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Reprint requests: Petra Mamic, MD, Medicine Residency Program, Stanford University School of Medicine, 300 Pasteur Drive, L154, Stanford, California 94305-5133. Tel.: +650 498 4560; Fax: +650 498 6205. E-mail: pmamic1@gmail.com.

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Nearly 6 million Americans live with heart failure (HF).[1] These patients are among the most frequently hospitalized, with 90-day readmission rates as high as 34%.[2] Though HF exacerbations and other cardiac events contribute significantly to the burden of hospitalizations, the leading causes of all hospitalizations are noncardiac.[3–5] Many of these are infections, with urinary tract infection (UTI), pneumonia (PNA), and sepsis[3–5] being the most common. As a result, patients with HF receive broad-spectrum antibiotics, which together with frequent hospitalizations and multiple comorbidities may place them at a higher risk of *Clostridium difficile* infection (CDI).

CDI is a potentially lethal disease in susceptible patients. The anaerobic Gram-positive spore-forming nosocomial pathogen may present with asymptomatic carriage and progress to fulminant colitis and death. Both incidence and severity of

CDI in the United States have been steadily increasing. From 1993 to 2003, the incidence and mortality of CDI have more than doubled—from 261 to 546 per 100,000 hospitalizations and from 20 to 50 per 100,000 hospitalizations, respectively.[6] In 2011, there were nearly half a million cases of CDI in the United States.[7]

Although some studies have shown that patients with HF may be at higher risk for CDI,[8–10] the rates of CDI in hospitalized patients with HF who have other bacterial infections (and are therefore receiving antibiotics) are not known. Similarly, the impact of CDI on in-hospital mortality for these patients is unknown. Understanding whether CDI is more likely to occur in patients with comorbid HF, and whether CDI portends a particularly poor prognosis in patients with HF, may help identify potential targets for intervention to improve outcomes in this population.

We hypothesized that hospitalized patients with HF diagnosed with and treated for other bacterial infections would have higher rates of CDI compared with hospitalized patients without HF who had the same infections. We also hypothesized that among the hospitalized patients with HF diagnosed with other bacterial infections, those with concomitant CDI would have higher in-hospital mortality.

Methods

Data Source

We used the 2012 National Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality (AHRQ), a nationally representative sample of inpatient hospitalizations in the United States. The 2012 dataset is the most recent year available at the time of publication. NIS is a sample of discharges from US community hospitals, which includes nonfederal, general, and specialty hospitals, and includes data on more than 7 million inpatient stays each year, which approximates a 20% stratified sample of US community hospitals.[11] The NIS database includes data on patient demographics and insurance status, hospital characteristics, diagnoses, and procedures. The unit of analysis in NIS is a patient hospitalization.

Study Population and Variable Definitions

We included all adult (age ≥18) hospitalizations with discharge diagnosis of UTI, PNA, or sepsis. We included hospitalizations with discharge diagnoses of bacterial infections because the documented presence of these infections was highly likely to involve antibiotic therapy, an important risk factor for CDI. We chose these particular infections because they are the most common infections in hospitalized patients with HF[3–5] as well as 3 of the 4 most common bacterial infections in all hospitalized patients.[12] These infections were defined as Clinical Classification Software (CCS) discharge diagnosis code 159 (UTI), 122 (PNA), or 2 (sepsis) in any position. CCS is an AHRQ tool used to collapse more than 17,000 diagnoses and procedure codes from the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) into a smaller number of clinically meaningful categories.[13]

Hospitalizations were divided into 2 groups: those with discharge diagnosis of HF and those without. HF was based on the following ICD-9-CM discharge diagnosis codes in any position: 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, or 428. These codes are recommended by the professional cardiology societies to define HF.[14,15] Although these codes have not been validated in the NIS database specifically, studies have shown that they can be used to rule in the diagnosis of HF using administrative data with high specificity.[16,17] Furthermore, this algorithm for ICD-9-CM coding was similar to well-validated algorithms used in several other studies.[16,18–20] We also included hospitalizations in this category if they had been assigned the AHRQ HF comorbidity (categorical variable CM_CHF in the NIS database). The correlation between these ICD-9-CM codes and the definition combining these codes with the AHRQ HF comorbidity was 99.94%.

Comorbidities were determined based on the assigned ICD-9-CM diagnostic codes, CCS codes, and AHRQ comorbidity variables. We included the following comorbidities: ischemic heart disease (IHD; ICD-9-CM code 410–414), hypertension (HTN; CCS code 98–99 or AHRQ variable CM_HTN_C), diabetes mellitus (DM; CCS code 49–50 or AHRQ variable CM_DM or CM_DMCX), chronic kidney disease (CKD; CCS code 158 or AHRQ variable CM_RENLFAIL), lung disease (CCS code 127–128 or 132 or AHRQ variable CM_CHRNLUNG), liver disease (CCS code 150–151 or AHRQ variable CM_LIVER), malignancy (CCS code 11–45 or AHRQ variable CM_TUMOR, CM_METS or CM_LYMPH), and anemia (CCS code 59–61 or AHRQ variable CM_ANEMDEF).

Patient characteristics and comorbidities as well as hospital characteristics were presented for all hospitalizations by HF status. They were also presented for the HF hospitalizations by CDI status. If there were any missing values for a variable, this was presented. CDI was defined as ICD-9-CM discharge diagnosis code 008.45 in any position. The rate of CDI was determined for hospitalizations with and without HF and displayed graphically. The rate of in-hospital mortality for hospitalizations with discharge diagnosis of HF was calculated by CDI status and displayed graphically. Both displays present information for all infections combined and separately by UTI, PNA, and sepsis.

Statistical Methods

Unadjusted and adjusted analyses were performed. The Student *t* test was used to compare continuous variables and the chi square test to compare categorical variables. All testing was 2-sided and performed at the 0.05 level of statistical significance. To produce national estimates, the data were weighted using survey weights provided by HCUP. All reported frequencies represent weighted values. Unadjusted comparisons were similarly conducted using weighted values.