CLINICAL RESEARCH STUDY

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Digoxin Use and Lower 30-day All-cause Readmission for Medicare Beneficiaries Hospitalized for Heart Failure

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ABSTRACT

BACKGROUND: Heart failure is the leading cause for hospital readmission, the reduction of which is a priority under the Affordable Care Act. Digoxin reduces 30-day all-cause hospital admission in chronic systolic heart failure. Whether digoxin is effective in reducing readmission after hospitalization for acute decompensation remains unknown.

METHODS: Of the 5153 Medicare beneficiaries hospitalized for acute heart failure and not receiving digoxin, 1054 (20%) received new discharge prescriptions for digoxin. Propensity scores for digoxin use, estimated for each of the 5153 patients, were used to assemble a matched cohort of 1842 (921 pairs) patients (mean age, 76 years; 56% women; 25% African American) receiving and not receiving digoxin, who were balanced on 55 baseline characteristics.

RESULTS: Thirty-day all-cause readmission occurred in 17% and 22% of matched patients receiving and not receiving digoxin, respectively (hazard ratio [HR] for digoxin, 0.77; 95% confidence interval [CI], 0.63-0.95). This beneficial association was observed only in those with ejection fraction <45% (HR 0.63; 95% CI, 0.47-0.83), but not in those with ejection fraction ≥45% (HR 0.91; 95% CI, 0.60-1.37; *P* for interaction, .145), a difference that persisted throughout the first 12 months postdischarge (*P* for interaction, .019). HRs (95% CIs) for 12-month heart failure readmission and all-cause mortality were 0.72 (0.61-0.86) and 0.83 (0.70-0.98), respectively.

CONCLUSIONS: In Medicare beneficiaries with systolic heart failure, a discharge prescription of digoxin was associated with lower 30-day all-cause hospital readmission, which was maintained at 12 months, and was not at the expense of higher mortality. Future randomized controlled trials are needed to confirm these findings.
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KEYWORDS: Digoxin; Heart failure; Hospital readmission

Heart failure is the leading cause of hospital admission and readmission for Medicare beneficiaries in the US.[1] Under the 2010 Patient Protection and Affordable Care Act, hospitals are collectively facing billions of dollars in penalties for excessive 30-day all-cause readmissions.[2] Since October 1, 2012, heart failure is 1 of the 3 conditions, along with acute

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Conflict of Interest: None.

Authorship: AA conceived the study hypothesis and design in collaboration with the coauthors. AA and KP wrote the first draft. AA and KP performed statistical analyses in collaboration with IBA, TEL, and CJM. All authors interpreted the data, participated in critical revision of the paper for important intellectual content, and approved the final version of the article. IBA, AA, CJM, and KP had full access to data.

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myocardial infarction and pneumonia, for which the law currently is being enforced.[2-4] Despite limitations of the cost-driven metric of 30-day all-cause hospital readmission,[5,6] the fact remains that over a quarter of heart failure patients are readmitted within 30 days of hospital discharge,[1] and that there is a need for interventions to improve this outcome. Studies of transition of care strategies in heart failure are based on single-center reports, post hoc analyses, and observational studies, and have shown variable and inconsistent associations with 30-day all-cause hospital readmission.[7]

Heart failure is a clinical syndrome characterized by fluid retention and shortness of breath, exacerbation of which often precedes hospitalization.[8,9] Digoxin has favorable hemodynamic and neuroendocrine effects in patients with heart failure.[10-12] Findings from the Randomized Assessment of Digoxin on Inhibitors of Angiotensin-Converting Enzyme (RADIANCE) trial and the Prospective Randomized Study of Ventricular Failure and the Efficacy of Digoxin (PROVED) trial, the 2 major randomized controlled trials of digoxin withdrawal in heart failure conducted in the early 1990s, demonstrated the beneficial effect of digoxin in reducing heart failure symptoms.[13,14] These findings were subsequently confirmed in the randomized controlled Digitalis Investigation Group (DIG) trial, which demonstrated that digoxin reduced the risk of hospitalization due to worsening heart failure in ambulatory patients with systolic heart failure during 37 months of average follow-up and in diastolic heart failure during the first 2 years of follow-up.[15,16]

Findings from post hoc analyses of the main DIG trial demonstrated that digoxin reduced 30-day all-cause hospital admission among ambulatory older patients with systolic heart failure,[17] and that the beneficial effect of digoxin on hospital admission in heart failure may be more pronounced in high-risk subsets of patients.[18] Based on these observations and that most evidence-based heart failure therapies that reduce hospital admission also reduce readmission,[19,20] we hypothesized that discharge prescription of digoxin will be associated with lower 30-day all-cause readmission in older heart failure patients hospitalized for acute decompensation. Therefore, the objective of the current study was to test the hypothesis that digoxin use is associated with lower 30-day all-cause hospital readmission.

CLINICAL SIGNIFICANCE

- Digoxin use was associated with lower risk of 30-day all-cause readmission without higher mortality in Medicare beneficiaries hospitalized for acute heart failure.
- This benefit of digoxin was observed throughout the first 12 months after discharge but appeared to be restricted to those with ejection fraction <45%.

MATERIALS AND METHODS

Data Source and Study Patients

The current study is based on the Alabama Heart Failure Project, the details of which have been described previously.[21,22] Briefly, 9649 medical records of 8555 unique fee-for-service Medicare beneficiaries discharged with a primary discharge diagnosis of heart failure from 106 Alabama hospitals between 1998 and 2001 were abstracted by trained technicians at the Clinical Data Abstraction Center. For patients with multiple hospitalizations, charts from the first hospitalization were used.[23] A diagnosis of heart failure was based on the *International Classification of Diseases*, 9th Revision, Clinical Modification codes for heart failure.[23] Of the 8555 patients, 8049 were discharged alive.

New Use of Digoxin: Assembly of an Inception Cohort

Data on admission and discharge digoxin use were collected by chart abstraction. Because prevalent drug use may cause bias through effects on baseline characteristics and by left censoring,[24,25] we excluded 2896 patients who were receiving digoxin at the time of hospital admission. Of the remaining 5153 patients without prior digoxin use, 1054 (20%) received a new discharge prescription for digoxin. Extensive data on other baseline characteristics including demographics, medical history, use of medications, hospital course, and discharge disposition also were collected by chart abstraction.[23]

Propensity Matching: Assembly of a Balanced Cohort

We used propensity score for the receipt of a discharge digoxin prescription to assemble a balanced matched cohort of patients receiving and not receiving digoxin.[26,27] Propensity scores for digoxin use were estimated for each of the 5153 patients using a nonparsimonious multivariable logistic regression model in which the digoxin use was the dependent variable and 55 baseline characteristics were used as covariates.[28-30] Using a greedy matching protocol described elsewhere,[31] we matched 921 (87% of the 1054) patients receiving digoxin with 921 patients not receiving digoxin with similar propensity scores. Postmatch balance in baseline characteristics was assessed by estimating absolute standardized differences, the results of which were presented as a Love plot.[32] An absolute standardized difference of 0% indicates no residual bias, and differences <10% are considered inconsequential.

Hospitalization and Mortality Data

The primary outcome of the current analysis was hospital readmissions due to all causes during 30 days after discharge from the index hospitalization. Secondary outcomes included hospital readmissions due to heart failure, all-cause mortality, and composite end point of all-cause