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Authors

Sheriff, Helen M
Thogaripally, Manik R
Panjrath, Gurusher
et al.

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Digoxin and 30-Day All-Cause Readmission in Long-Term Care Residents Hospitalized for Heart Failure

Helen M. Sheriff, MD[1,*], **Manik R Thogaripally, BS**[2,*], **Gurusher Panjrath, MD**[3], **Cherinne Arundel, MD**[1,3], **Qing Zeng, PhD**[1,3], **Gregg C. Fonarow, MD**[4], **Javed Butler, MD**[5], **Ross D. Fletcher, MD**[1,6], **Charity Morgan, PhD**[2], **Marc R. Blackman, MD**[1,3,6], **Prakash Deedwania, MD**[7], **Thomas E. Love, PhD**[8], **Wilbert S. Aronow, MD**[9], **Stefan D. Anker, MD, PhD**[10,11], **Richard M. Allman, MD**[12], and **Ali Ahmed, MD, MPH**[1,2,3]

[1]Veterans Affairs Medical Center, Washington, DC

[2]University of Alabama at Birmingham, Birmingham, AL

[3]George Washington University, Washington, DC

[4]University of California, Los Angeles, CA

[5]State University of New York, Stony Brook, NY

[6]Georgetown University, Washington, DC

[7]University of California, San Francisco, Fresno, CA

[8]Case Western Reserve University, Cleveland, OH

[9]Westchester Medical Center and New York Medical College, Valhalla, NY

[10]Department of Cardiology and Pneumology, University Medicine Göttingen (UMG), Göttingen, Germany & DZHK (German Center for Cardiovascular Research)

[11]Division of Cardiology and Metabolism – Heart Failure, Cachexia & Sarcopenia; Department of Cardiology (CVK); and Berlin-Brandenburg Center for Regenerative Therapies (BCRT), at Charité University Medicine, Berlin, Germany

[12]Department of Veterans Affairs, Geriatrics and Extended Care Services, Washington, DC

Abstract

Background—Digoxin has been shown to be associated with a lower risk of 30-day all-cause hospital readmissions in older patients with heart failure (HF). In the current study, we examined this association among long-term care (LTC) residents hospitalized for HF.

Correspondence: Ali Ahmed, MD, MPH, Center for Health and Aging, Washington DC VA Medical Center, 50 Irving St. NW, Washington, DC 20422; Telephone: 1-202-745-8386; aliahmedmdmph@gmail.com.

*Joint first authors

Methods—Of the 8049 Medicare beneficiaries discharged alive after hospitalization for HF from 106 Alabama hospitals, 545 (7%) were LTC residents, of which 227 (42%) received discharge prescriptions for digoxin. Propensity scores for digoxin use, estimated for each of the 545 patients, were used to assemble a matched cohort of 158 pairs of patients receiving and not receiving digoxin who were balanced on 29 baseline characteristics. Hazard ratios (HR) and 95% confidence intervals (CI) for outcomes associated with digoxin among matched patients were estimated using Cox regression models.

Results—Matched patients (n=316) had a mean age of 83 years, 74% were women, and 18% African American. 30-day all-cause readmission occurred in 21% and 20% of patients receiving and not receiving digoxin, respectively (HR, 1.02; 95% CI, 0.63–1.66). Digoxin had no association with allcause mortality (HR, 0.90; 95% CI, 0.48–1.70), HF readmission (HR, 0.90; 95% CI, 0.38–2.12) or combined endpoint of all-cause readmission or all-cause mortality (HR, 0.97; 95% CI, 0.65–1.45) at 30 days. These associations remained unchanged at 1 year post-discharge.

Conclusions—The lack of an association between digoxin and 30-day all-cause readmission in older nursing home residents hospitalized for HF is intriguing and needs to be interpreted with caution given the small sample size.

Keywords

Digoxin; nursing home; heart failure; hospital readmission

Heart failure (HF) is the leading cause for hospital readmission for Medicare beneficiaries.[1] Reduction of 30-day all-cause hospital readmission is a focus of the Affordable Care Act.[2] Digoxin has been shown to reduce the risk of 30-day all-cause hospital readmission in real-world older HF patients.[3,4] HF is common in nursing homes.[5] However, whether digoxin is effective in lowering 30-day all-cause readmission in hospitalized HF patients admitted from long-term care (LTC) facilities remains unclear. In the current study we examined if digoxin use is associated with a lower 30-day all-cause hospital readmission in a propensity score-matched cohort of LTC residents with HF.[6]

Methods

Data source and study patients

Data from the Alabama Heart Failure Project were used for the current analysis, the design and methods of which have been previously described.[3,7–9] Briefly, 9649 medical records of 8555 unique fee-for-service Medicare beneficiaries discharged between 1998 and 2001 from 106 Alabama hospitals with a primary discharge diagnosis of HF were abstracted by trained data abstractors using structured data collection tools.[7] ICD-9 codes for HF were used to identify patients with a primary discharge diagnosis of HF. Of the 8049 Medicare beneficiaries discharge alive, 545 (7%) were admitted form the LTC settings.

Discharge prescription for digoxin

The primary exposure in our analysis was the receipt of a prescription of digoxin before hospital discharge. Of the 545 patients admitted form LTC settings, 227 (42%) received discharge prescriptions for digoxin. As mentioned above, data on both admission and

discharge use of digoxin were centrally collected by trained chart abstractors.[7] Given the small number of patients admitted from the LTC, we did not assemble an inception cohort of new-users of digoxin by excluding patients who were receiving digoxin before hospital admission.[3] Because of our aim to determine if the prior findings of the clinical effectiveness of digoxin in lowering 30-day all-cause readmission can be confirmed in patients admitted from the LTC settings and their small sample size,[3] we included all HF patients regardless of their ejection fraction (EF), with a plan to conduct subgroup analysis and check for effect modification. Extensive data were abstracted on demographics, various baseline characteristics including past medical history and pre-admission medication use, in-hospital care, and discharge medication.

Outcomes

The primary outcome of the current analysis is 30-day all-cause readmissions from the day of hospital discharge. Data on hospitalization and time to hospitalization were obtained from the CMS Medicare Provider Analysis and Review (MedPAR) file that also contains data on services provided to Medicare beneficiaries from the time of admission to inpatient hospitals through discharge. Our secondary outcomes included 30-day HF readmission and all-cause mortality, as well as 1-year postdischarge outcomes. Considering the very high risk of death in hospitalized HF patients admitted from the LTC settings, to account for the competing risk of death on readmission, we also estimated composite end points of all-cause readmissions or all-cause mortality. Data on mortality and time of death were obtained from the CMS Denominator File that contains data on all Medicare beneficiaries enrolled and/or entitled in a given year including their dates of birth and death.[7–9]

Assembly of a balanced cohort: Propensity score matching

Because digoxin is often prescribed for sicker patients who may have poorer outcomes, to minimize bias associated with indication of digoxin prescription, we used propensity scores or the conditional probability for the receipt of a digoxin prescription prior to discharge to assemble a matched cohort of patients in which those receiving and not receiving digoxin would be well balanced on key measured baseline characteristics.[10,11] Propensity scores for the receipt of digoxin use were estimated for each of the 545 patients using a non-parsimonious multivariable logistic regression model in which the receipt of digoxin was the dependent variable and 29 baseline characteristics were used as covariates.[12–14] Using a greedy matching protocol described elsewhere,[15] we assembled a matched cohort of 158 pairs of patients receiving and not receiving digoxin. To estimate if the 29 baseline characteristics used in the propensity score model were sufficiently balanced between the two groups, we estimated absolute standardized differences for all those variables.[16] An absolute standardized difference of 0% indicates no residual bias and differences <10% are considered inconsequential.

Statistical analysis

Descriptive analyses comparing between-group baseline characteristics were conducted using Pearson’s Chi-square and Wilcoxon rank-sum tests as appropriate. To examine the association of digoxin use with 30-day all-cause readmission, we used Kaplan-Meier and Cox regression analyses, censoring all patients without an event at 30 days. A significant

association of digoxin use with the primary outcome of 30-day all-cause readmission among matched patients will be tested using a formal sensitivity analysis to quantify the degree of a hidden bias for an unmeasured confounder.[17] All other associations were examined using similar Cox models. We also examined the association of digoxin with 30-day outcomes in the pre-match cohort using a multivariable-adjusted model using all 29 baseline characteristics and the propensity scores. All statistical tests were two-tailed with a p-value <0.05 considered significant. SPSS for Windows version 21 (IBM Corp., Armonk, NY) used for data analyses.

Results

Baseline characteristics

Matched patients (n=316) had a mean age of 83 (±8) years, 74% were women and 18% were African American. Before matching, patients receiving digoxin were more likely to have low EF, prior history of HF, atrial fibrillation, and dementia. They were also more likely to receive diuretics and angiotensin-converting enzyme (ACE) inhibitors. These and other imbalances were balanced after matching (Table 1 and Figure 1).

30-day all-cause readmission

30-day all-cause hospital readmission occurred in 21% (33/158) and 20% (32/158) of matched patients receiving and not receiving a discharge digoxin prescription, respectively (hazard ratio {HR} when digoxin use was compared with its non-use, 1.02; 95% confidence interval {CI}, 0.63–1.66; p=0.935; Table 2). Among the subset of 79 matched patients with EF <45%, 30-day all-cause readmission occurred in 30% and 13% of those receiving and not receiving digoxin, respectively (HR, 2.54; 95% CI, 0.89–7.21; P=0.080). Among the subset of 96 matched patients with atrial fibrillation, 30-day all-cause readmission occurred in 20% of patients in each of the digoxin and non-digoxin groups, respectively (HR, 1.04; 95% CI, 0.42–2.55; P=0.938). Among the subset of 220 matched patients with normal sinus rhythm, 30-day all-cause readmission occurred in 21% of patients in each of the digoxin and non-digoxin groups, respectively (HR, 1.00; 95% CI, 0.56–1.79; P=0.991).

Among the 545 pre-match patients, multivariable-adjusted and propensity score adjusted HRs (95% CIs) associated with digoxin prescription for 30-day all-cause readmission were 1.22 (0.80–1.84; p=0.356) and 1.20 (0.79–1.82; p=0.383), respectively. Among the subset of 122 pre-match patients with EF <45%, HR for 30-day all-cause readmission associated with digoxin use was 6.51 (95% CI, 1.67–25.31; P=0.007).

Other 30-day outcomes

30-day all-cause mortality occurred in 11% (18/158) and 13% (20/158) of patients receiving and not receiving digoxin, respectively (HR, 0.90; 95% CI, 0.48–1.70; p=0.742). Consequently, digoxin use had no association with the combined end point of all-cause mortality or all-cause readmission during 30 days post-discharge (HR, 0.97; 95% CI, 0.65–1.45; p=0.876; Table 2 and Figure 2). Digoxin use had no association with HF readmission.

12-month outcomes

Digoxin use had no association with all-cause or HF readmission, all-cause mortality, or the combined end point of all-cause mortality or all-cause readmission during 1 year post-discharge (Table 3).

Discussion

Findings from our current analyses demonstrate that there is no evidence that a discharge prescription of digoxin is associated with a lower risk of 30-day all-cause readmission among older LTC residents hospitalized for decompensated HF. Digoxin use also had no association with 30-day all-cause mortality or HF readmission. We also observed that all associations remained non-significant for 1-year outcomes. These associations based on a balanced propensity-matched cohort are consistent with risk-adjusted findings from the larger pre-match cohort, and suggest that digoxin, a drug known for its beneficial effect and effectiveness on hospital admission and readmission in both randomized controlled trials and in the real-world settings, had no such association with readmission in real-world LTC residents with HF.

The lack of an association of digoxin use with outcomes in HF patients admitted from the LTC facility is somewhat intriguing. Although LTC residents with HF would be expected to avoid symptoms by restricting their mobility, their 30-day readmission rate was very similar to the one observed for older HF patients in general.[18] Digoxin is known for its beneficial effects in high risk subset of HF patients.[19] And, yet we found no beneficial association of digoxin with readmission in nursing home residents. There are several potential explanations for this lack of association. Digoxin is known for its lower efficacy in women with HF and nearly three quarters of the HF patients admitted from LTC in our study were women.[20–22] Digoxin is also known for its greater efficacy in patients with HF and reduced EF.[3,4] Only about a quarter of the matched patients in our study had low EF. However, we found a trend toward higher risk for 30-day all-cause readmission when we repeated our analysis in the subset of prematch patients with low EF. A higher comorbidity burden in older LTC residents with HF and the competing risks associated with these comorbidities may have cancelled any potential readmission benefit of digoxin use.[23,24] Nearly half of the older Medicare beneficiaries with HF have 5 or more other chronic morbidities,[25] and these numbers would be expected to be higher in the LTC setting. This is especially important as less than half of all readmissions were due to HF. Finally, our study may be underpowered to detect an association of digoxin use with outcomes. However, when patients were followed up for 12 months post-discharge, nearly 60% were readmitted and over 80% experienced one of the combined end point events of readmission or death due to any cause, there was no association of digoxin with any 12-month outcomes.

Findings of our study are important. Digoxin is an inexpensive drug known for its efficacy and effectiveness in lowering readmission rates in patients with HF the reduction of which is a focus of the Affordable Care Act.[1,2,4,18] Because HF is common in the LTC setting, clinicians might be tempted to prescribe digoxin to their HF patients to reduce the risk of hospital readmission. However, finding from our study suggest that there is no evidence of a beneficial association of digoxin with readmission in the patients. Clinicians should use

caution about the routine use of digoxin and may consider other approaches such as better transitions of care and judicious use of diuretics.[26,27]

Our study is limited by its small sample size and the observational design. Bias due to residual confounding from a measured covariate or confounding from a hidden covariate is possible. Because of the null association observed in our study, we were not able to perform a formal sensitivity analysis. We also had no data on post-discharge adherence and regression dilution from crossover of treatment during follow-up may also explain the null associations.[28]. Finally, our study in based on fee-for-service Medicare beneficiaries from a single state during 1999–2001 with only 20% receiving beta-blockers may limit generalizability.

In conclusion, Medicare beneficiaries who are hospitalized from the LTC for decompensated HF, there is no evidence of any association between digoxin use and 30-day or 1-year all-cause or HF readmission. These findings suggest that digoxin should not be routinely use for lowering the risk of 30-day all-cause readmission in these patients. Future studies with larger sample size and more contemporary HF patients from the LTC setting are needed to determine the role of digoxin in hospitalized HF patients admitted from the LTC setting.

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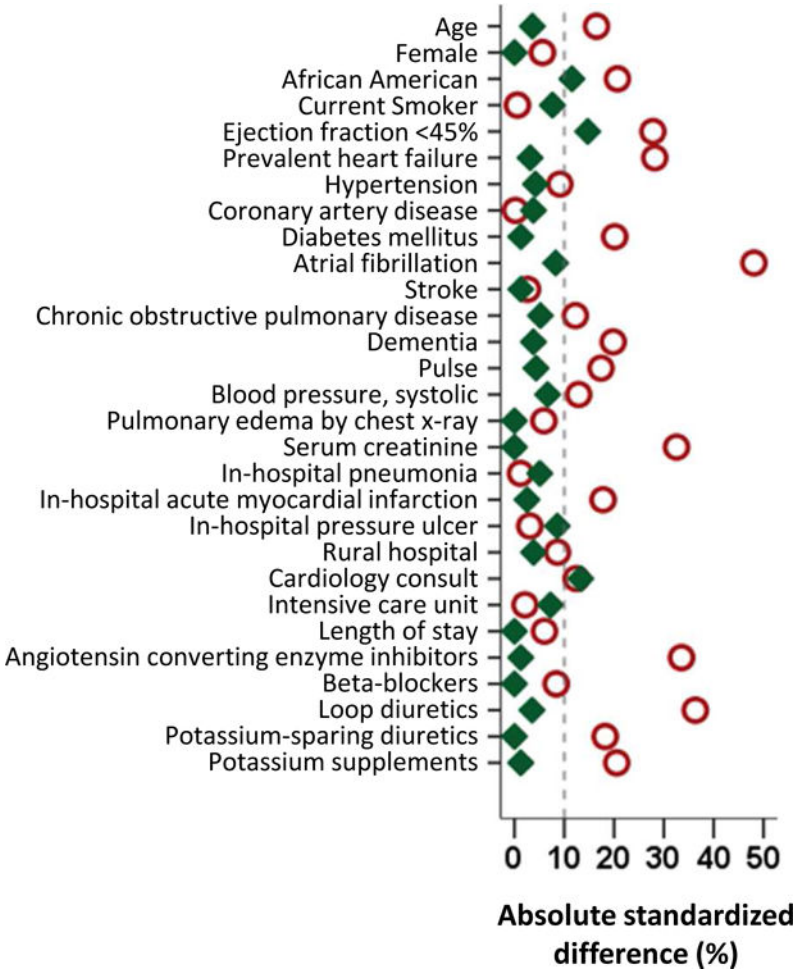

Figure 1.

Love plot displaying absolute standardized differences for 29 baseline characteristics between patients receiving and not receiving digoxin, before and after propensity score matching are indicated by blank circle and black diamond shapes; ACE= Angiotensin converting enzyme

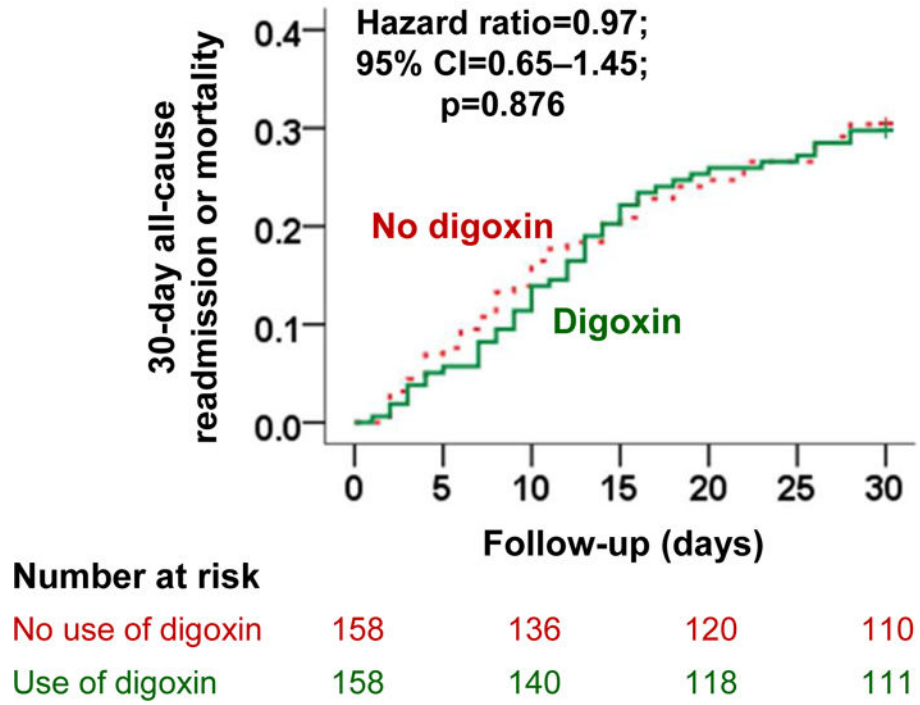

Figure 2.

Kaplan-Meier plots for the combined end point of 30-day all-cause hospital readmission or 30-day all-cause mortality in a propensity-matched cohort of older heart failure patients admitted from nursing homes receiving and not receiving a discharge prescription for digoxin (CI=confidence interval)

Table 1

Baseline characteristics of nursing home residents hospitalized for decompensated heart failure, by discharge prescription for digoxin, before and after propensity score matching

n (%) or mean (±SD)	Pre-match (N=545)			Post-match (N=316)		
	Use of digoxin		P value	Use of digoxin		P value
	No (n=318)	Yes (n=227)		No (n=158)	Yes (n=158)	
Age (years)	82 (±9)	84 (±8)	0.061	83 (±8)	83 (±9)	0.700
Female	239 (75%)	165 (73%)	0.516	117 (74%)	117 (74%)	1.000
African American	70 (22%)	32 (14%)	0.020	32 (20%)	25 (16%)	0.306
Current smoker	15 (5%)	11 (5%)	0.945	12 (8%)	9 (6%)	0.498
Left ventricular ejection fraction (%)						
≥45%	103 (32%)	46 (20%)	<0.001	44 (28%)	34 (22%)	0.406
<45%	51 (16%)	71 (31%)		39 (25%)	40 (25%)	
Unknown	164 (52%)	110 (49%)		75 (48%)	84 (53%)	
Past medical history						
Prior heart failure	226 (71%)	188 (83%)	0.002	125 (79%)	127 (80%)	0.780
Hypertension	215 (68%)	163 (72%)	0.295	112 (71%)	115 (73%)	0.708
Coronary artery disease	146 (46%)	104 (46%)	0.982	73 (46%)	76 (48%)	0.735
Myocardial infarction	58 (18%)	41 (18%)	0.958	34 (22%)	31 (20%)	0.676
Angina pectoris	28 (9%)	25 (11%)	0.391	18 (11%)	18 (11%)	1.000
Left bundle branch block	26 (8%)	26 (12%)	0.199	15 (10%)	18 (11%)	0.581
Percutaneous coronary intervention	23 (7%)	16 (7%)	0.934	11 (7%)	14 (9%)	0.532
Coronary artery bypass graft	38 (12%)	28 (12%)	0.892	18 (11%)	19 (12%)	0.861
Diabetes mellitus	152 (48%)	86 (38%)	0.021	66 (42%)	67 (42%)	0.909
Atrial fibrillation	62 (19%)	93 (41%)	<0.001	51 (32%)	45 (29%)	0.463
Stroke	122 (38%)	90 (40%)	0.762	63 (40%)	62 (39%)	0.908
Chronic obstructive pulmonary disease	106 (33%)	89 (39%)	0.158	58 (37%)	62 (39%)	0.643
Dementia	134 (42%)	118 (52%)	0.023	78 (49%)	75 (48%)	0.736
Clinical findings						
Pulse (beats per minute)	90 (±22)	94 (±24)	0.061	92 (±22)	93 (±24)	0.729

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n (%) or mean (±SD)	Pre-match (N=545)			Post-match (N=316)		
	Use of digoxin		P value	Use of digoxin		P value
	No (n=318)	Yes (n=227)		No (n=158)	Yes (n=158)	
Systolic blood pressure (mmHg)	146 (±32)	142 (±30)	0.072	141 (±30)	143 (±30)	0.585
Diastolic blood pressure (mmHg)	75 (±19)	75 (±19)	0.981	75 (±20)	75 (±18)	0. 901
Lower extremity edema	204 (64)	148 (66)	0.801	100 (63)	103 (65)	0.725
Pulmonary edema by chest x-ray	262 (82)	192 (85)	0.499	132 (84)	132 (84)	1.000
Laboratory values						
Serum sodium (mEq/L)	139 (±5)	138 (±7)	0.311	139 (±5)	139 (±7)	0.569
Serum potassium (mEq/L)	4.5 (±0.8)	4.4 (±0.7)	0.348	4.5 (±0.8)	4.4 (±0.7)	0.328
Serum creatinine (mEq/L)	1.6 (±1.1)	1.3 (±0.7)	0.003	1.4 (±0.7)	1.4 (±0.7)	0.905
Hematocrit (%)	35 (±6)	36 (±6)	0.143	35 (±6)	36 (±6)	0.392
In-hospital events						
Pneumonia	141 (44%)	102 (45%)	0.891	72 (46%)	68 (43%)	0.651
Acute myocardial infarction	11 (4%)	17 (8%)	0.036	11 (7%)	10 (6%)	0.821
Pressure ulcer	87 (27%)	59 (26%)	0.722	45 (29%)	39 (25%)	0.445
Hospital and care characteristics						
Rural hospital	121 (38%)	96 (42%)	0.319	70 (44%)	67 (42%)	0.733
Cardiology consult	95 (30%)	81 (36%)	0.153	60 (38%)	50 (32%)	0.238
Intensive care unit	11 (4%)	7 (3%)	0.809	4 (3%)	6 (4%)	0.520
Length of stay (days)	7 (±6)	7 (±5)	0.492	7 (±6)	7 (±4)	0.658
Discharge medications						
ACE inhibitors or ARBs	124 (39%)	126 (56%)	<0.001	80 (51%)	79 (50%)	0.910
Beta-blockers	58 (18%)	49 (22%)	0.332	30 (19%)	30 (19%)	1.000
Loop diuretics	232 (73%)	198 (87%)	<0.001	133 (84%)	135 (85%)	0.754
Potassium-sparing diuretics	30 (9%)	35 (15%)	0.034	17 (11%)	17 (11%)	1.000
Potassium supplements	126 (40%)	113 (50%)	0.018	75 (48%)	76 (48%)	0.910

Table 2

30-day outcomes by discharge prescription for digoxin in the propensity-matched cohort

Outcomes	% (events)		Absolute risk difference*	Hazard ratio† (95% confidence interval)	P value
	New discharge prescription for digoxin				
	No (n=158)	Yes (n=158)			
All-cause hospital readmission	32 (20%)	33 (21%)	1%	1.02 (0.63–1.66)	0.935
Heart failure hospital readmission	11 (7%)	10 (6%)	−1%	0.90 (0.38–2.12)	0.809
All-cause mortality	20 (13%)	18 (11%)	−2%	0.90 (0.48–1.70)	0.742
All-cause mortality or all-cause hospital readmission	48 (30%)	47 (30%)	1%	0.97 (0.65–1.45)	0.876

*Absolute risk differences were calculated by subtracting percent events in patients receiving no digoxin from those receiving those drugs

†The hazard ratios compared patients receiving digoxin versus those not receiving digoxin

Table 3

1-year outcomes by discharge prescription for digoxin in the propensity-matched cohort

Outcomes	% (events)		Absolute risk difference*	Hazard ratio† (95% confidence interval)	P value
	New discharge prescription for digoxin				
	No (n=158)	Yes (n=158)			
All-cause hospital readmission	95 (60%)	91 (58%)	−2%	0.98 (0.74–1.31)	0.896
Heart failure hospital readmission	38 (24%)	29 (18%)	−6%	0.77 (0.48–1.25)	0.293
All-cause mortality	92 (58%)	99 (63%)	5%	1.10 (0.83–1.46)	0.516
All-cause mortality or all-cause hospital readmission	133 (84%)	134 (85%)	1%	1.03 (0.81–1.31)	0.830

*Absolute risk differences were calculated by subtracting percent events in patients receiving no digoxin from those receiving those drugs

†The hazard ratios compared patients receiving digoxin versus those not receiving digoxin.