ORIGINAL RESEARCH

Hospital Variation of Spironolactone Use in Patients Hospitalized for Heart Failure in China—The China PEACE Retrospective Heart Failure Study

Yuan Yu, MD, PhD; Wenchi Guan, MD, PhD; Frederick A. Masoudi, MD, MSPH; Bin Wang, MD, PhD; Guan He, MD, PhD; John A. Spertus, MD; Yuan Lu, ScD; Harlan M. Krumholz, MD, SM*; Jing Li, MD, PhD*

BACKGROUND: Although aldosterone antagonists improve outcomes in select individuals with heart failure and reduced ejection fraction, studies in the United States have raised concerns about underuse and overuse. Variations in the prescription of aldosterone antagonist in China are unknown.

METHODS AND RESULTS: In the multicenter, hospital-based, retrospective China PEACE (China Patient-Centered Evaluative Assessment of Cardiac Events) study, we identified a nationally representative cohort of admissions for heart failure in a nationally representative sample of Chinese hospitals in 2015. Patients were classified into 1 of 3 groups according to their eligibility for spironolactone—"ideal" (left ventricular ejection fraction <40% and without contraindications), "contraindicated" (a documented contraindication, irrespective of left ventricular ejection fraction), and "uncertain-benefit" (all others). We measured hospital variation of spironolactone prescriptions at discharge in the "ideal" and "contraindicated" group and calculated the median odds ratio (MOR), a measure of institution-level variation for 2 individuals with similar characteristics discharged at 2 randomly selected hospitals. Hospital characteristics associated with spironolactone use were identified using multivariable linear regression model. Among 1222 ideal patients from 97 hospitals, the median rate of spironolactone prescription was 78.6% (interquartile range [IQR], 42.8%–99.6% [range, 0%–100%], MOR, 3.4 [95% CI, 2.7–4.0]) at discharge. Among 900 contraindicated patients from 83 hospitals, the median rate of spironolactone prescription was 30.0% (IQR, 9.1%–50.0% [range, 0%–100%], MOR, 3.1 [95% CI, 2.4–3.9]) at discharge. Hospitals with independent departments of cardiology and located in Eastern China were associated with a 38.0% (95% CI, 18.7–57.3; P<0.001) and a 14.6% (95% CI, 2.3%–26.9%; P=0.020) higher rate of spironolactone use for ideal patients.

CONCLUSIONS: In this national study of hospitals in China, the use of spironolactone among ideal patients and the inappropriate use of spironolactone among patients with contraindications was substantial, with rates that varied markedly by institution.

REGISTRATION: URL: https://www.clinicaltrials.gov. Unique identifier: NCT02877914.

Key Words: China ■ heart failure ■ quality of care ■ spironolactone

Aldosterone antagonists (AAs) reduce mortality for patients with heart failure (HF) and reduced ejection fraction and are strongly recommended for some patients in clinical guidelines.1–4 Patient selection is critical because AAs can cause life-threatening hyperkalemia or renal insufficiency in individuals with significant...
Yu et al  Hospital Variation of Spironolactone Use in HF

renal dysfunction or baseline hyperkalemia. Prior studies in the United States have identified both underuse of AAs among individuals who might benefit and overuse among those who are at risk for adverse consequences. This pattern of use substantially compromises the population benefits that might be attained with the integration of this therapy in practice.

Little is known about the national practice patterns of evidence-based spironolactone use in patients hospitalized for HF in China, where spironolactone is the only AA approved by the China Food and Drug Administration and inexpensive and readily available nationwide. Quality of care for HF varied substantially among hospitals in China, which suggests opportunities of improvement at the hospital level. However, little is known about the hospital variation in spironolactone use. Prior studies have reported the relatively high use of spironolactone in patients with HF in China. Few efforts have been devoted to the appropriate use and unsafe use of spironolactone according to the indications and contraindications and hospital-level factors associated with appropriateness of use.

Accordingly, we conducted a comprehensive quality assessment of spironolactone use, with data collected in the China PEACE 5r-HF (China Patient-Centered Evaluative Assessment of Cardiac Events Retrospective Study of Heart Failure). The study has identified a representative sample of hospitals in China and a large nationally representative sample of HF admissions in 2015. Our objectives were to describe the variation in spironolactone use among ideal and contraindicated patients at discharge and identify hospital characteristics associated with the appropriateness of spironolactone use.

**CLINICAL PERSPECTIVE**

**What is New?**
- In this national study of hospitals in China, we found that about 1 in 4 patients who were ideal candidates for spironolactone therapy were not treated and almost 1 in 3 with a contraindication to spironolactone were treated.
- Both underuse and inappropriate use of spironolactone varied markedly by hospital.

**What are the Clinical Implications?**
- These findings suggest a national strategy to improve more-appropriate use of spironolactone and an urgent need for identifying local barriers to evidence-based therapies in China.

**Nonstandard Abbreviations and Acronyms**

| Acronym     | Definition                                    |
|-------------|-----------------------------------------------|
| AA          | aldosterone antagonists                       |
| China PEACE 5r-HF | China Patient-Centered Evaluative Assessment of Cardiac Events Retrospective Study of Heart Failure |
| MOR         | median odds ratio                             |
| NYHA        | New York Heart Association                    |
| RALES       | Randomized Aldactone Evaluation Study         |

**METHODS**

The study materials have been made available to other researchers for purposes of replicating the procedure. It is our goal to share the prospective China PEACE 5r-HF data; however, at this time, we are unable to do so.

**Study Design of China PEACE 5r-HF Study**

China PEACE 5r-HF developed a 2-stage random sampling design to create a nationally representative sample of hospital admissions for HF. Briefly, we first identified a nationally representative cohort of 189 hospitals providing care for acute HF in China. Then, from the local hospital database of each sampled hospital, we employed systematic random sampling procedures to select 10,004 patients aged 18 years or older, hospitalized from January 1, 2015, to December 31, 2015, with a principal discharge diagnosis of HF. We used centralized data abstraction of in-hospital medical records with standardized definitions to ensure data accuracy. Details of the study design have been published.

Informed consent was waived for patients because the study only consisted of a review of medical records. The central ethics committee at the Chinese National Center for Cardiovascular Diseases and Yale University Human Investigation Committee approved the study. All collaborating hospitals accepted central ethics approval with the exception of 15 hospitals, which obtained local approval by their internal ethics committees. The study is registered at www.clinicaltrials.gov (NCT02877914).

**Study Samples and Definition of Patient Groups**

We limited study samples to patients who had sufficient opportunity to receive spironolactone, namely, those who had a length of stay of no less than 24 hours.
In addition, patients who died or withdrew medical treatment because of terminal status during hospitalization were excluded. Subsequently, we classified patients into 1 of 3 groups according to the recommendation of clinical guidelines:1–4 (1) the “ideal” group consisted of patients with documented left ventricular ejection fraction (LVEF) <40% and no contraindications to spironolactone; (2) the “contraindicated” group consisted of patients with a contraindication including renal dysfunction (serum creatinine >2.5 mg/dL in men or >2.0 mg/dL in women), hyperkalemia (potassium >5.0 mEq/L), or documented allergy to spironolactone, irrespective of LVEF; and (3) the “uncertain-benefit” group consisted of patients without contraindications but with undocumented LVEF or LVEF ≥40%.

Variables
Patient demographics, clinical characteristics at admission or discharge, medical history, comorbidities, laboratory tests, and treatments were abstracted from medical records.13 We collected LVEF values that were assessed during hospitalization or no longer than 1 month before admission. Hospital characteristics were obtained from a hospital survey, including teaching status, medical university affiliation, number of beds, whether they had a catheterization laboratory, independent department of cardiology, and capability to perform coronary artery bypass graft. Hospitals were classified according to their government-defined level in 2015: secondary hospitals have at least 100 inpatient beds and the capacity to treat local populations of at least 100,000, whereas tertiary hospitals are larger centers that provide more advanced care.

Outcome Measures
The primary outcome measures were spironolactone prescription in the “ideal” group and the “contraindicated” group at discharge. The secondary outcome measures were spironolactone prescription in the ideal group and in the contraindicated group during hospitalization. To capture the laboratory test results likely to influence the decision of spironolactone prescriptions at discharge, we used the last laboratory values before discharge. In evaluating spironolactone use during hospitalization, for patients who received spironolactone, we used the last laboratory values before administration of medication; for patients who ultimately did not receive spironolactone, we used the highest laboratory value recorded during hospitalization to ensure the identification of any possible contraindication.

Statistical Analysis
We calculated the proportions of patients who received spironolactone prescriptions during hospitalization and at discharge among patients of different categories. We reported percentages to describe categorical variables and medians with interquartile ranges (IQRs) to describe continuous variables. We then compared patient characteristics by prescription of spironolactone in the ideal and contraindicated groups at discharge, respectively, using chi-square tests for categorical variables and Kruskal-Wallis test for continuous variables. Additionally, we compared the proportions of patients who received spironolactone prescriptions among ideal and contraindicated patients by hospital subtype.

To describe institutional-level variation in spironolactone prescriptions in the ideal and contraindicated groups at discharge, we assessed the median and IQR of spironolactone prescriptions. In this analysis, hospitals with <5 eligible patients for the group of interest (ideal or contraindicated) were excluded. We then used Spearman correlation to estimate the correlation in hospital-level spironolactone prescription between the ideal and contraindicated groups. To determine the effects of institutional variation in spironolactone prescriptions from the ideal and contraindicated groups, we used hierarchical logistic regression to calculate the median odds ratio (MOR). An MOR, eg, of 2.0, indicates that the odds of receiving a spironolactone prescription would be 2-fold higher for 2 patients with identical characteristics discharged from one random hospital versus another. Models were adjusted for patient characteristics and a random effect at the institutional level to account for the patients’ clustering within hospitals, with backward stepwise selection of covariates that were significant at the 0.05 level. We selected explanatory variables based on the clinical judgment and review of the literature, including demographics, comorbidities, heart rate, systolic and diastolic blood pressure, HF-related symptoms, New York Heart Association (NYHA) classification, and laboratory tests. Based on previous literature, an MOR >1.2 indicates significant practice-level variation.6 We used the intraclass coefficient (ICC) to estimate the proportion of variance in spironolactone prescriptions that was attributable to between-hospital variations. We calculated the ICC from these hierarchical logistic models using the following equation: ICC = se²/(se² + (π²)/3), where se is the standard error of the random hospital intercept.14

To examine associations between hospital characteristics and rate of spironolactone prescription in the ideal and contraindicated patients at discharge, we divided hospitals into tertiles based on their respective rates (with the bottom tertile containing hospitals with the lowest rates and the top tertile containing hospitals with the highest rates). Within each rate tertile, a proportion was calculated for each categorical hospital characteristic and a median was calculated for each continuous hospital characteristic. To examine whether hospital

Yu et al  Hospital Variation of Spironolactone Use in HF

Statistical Analysis
We calculated the proportions of patients who received spironolactone prescriptions during hospitalization and at discharge among patients of different categories. We reported percentages to describe categorical variables and medians with interquartile ranges (IQRs) to describe continuous variables. We then compared patient characteristics by prescription of spironolactone in the ideal and contraindicated groups at discharge, respectively, using chi-square tests for categorical variables and Kruskal-Wallis test for continuous variables. Additionally, we compared the proportions of patients who received spironolactone prescriptions among ideal and contraindicated patients by hospital subtype.

To describe institutional-level variation in spironolactone prescriptions in the ideal and contraindicated groups at discharge, we assessed the median and IQR of spironolactone prescriptions. In this analysis, hospitals with <5 eligible patients for the group of interest (ideal or contraindicated) were excluded. We then used Spearman correlation to estimate the correlation in hospital-level spironolactone prescription between the ideal and contraindicated groups. To determine the effects of institutional variation in spironolactone prescriptions from the ideal and contraindicated groups, we used hierarchical logistic regression to calculate the median odds ratio (MOR). An MOR, eg, of 2.0, indicates that the odds of receiving a spironolactone prescription would be 2-fold higher for 2 patients with identical characteristics discharged from one random hospital versus another. Models were adjusted for patient characteristics and a random effect at the institutional level to account for the patients’ clustering within hospitals, with backward stepwise selection of covariates that were significant at the 0.05 level. We selected explanatory variables based on the clinical judgment and review of the literature, including demographics, comorbidities, heart rate, systolic and diastolic blood pressure, HF-related symptoms, New York Heart Association (NYHA) classification, and laboratory tests. Based on previous literature, an MOR >1.2 indicates significant practice-level variation.6 We used the intraclass coefficient (ICC) to estimate the proportion of variance in spironolactone prescriptions that was attributable to between-hospital variations. We calculated the ICC from these hierarchical logistic models using the following equation: ICC = se²/(se² + (π²)/3), where se is the standard error of the random hospital intercept.14

To examine associations between hospital characteristics and rate of spironolactone prescription in the ideal and contraindicated patients at discharge, we divided hospitals into tertiles based on their respective rates (with the bottom tertile containing hospitals with the lowest rates and the top tertile containing hospitals with the highest rates). Within each rate tertile, a proportion was calculated for each categorical hospital characteristic and a median was calculated for each continuous hospital characteristic. To examine whether hospital characteristics and a random effect at the institutional level to account for the patients’ clustering within hospitals, with backward stepwise selection of covariates that were significant at the 0.05 level. We selected explanatory variables based on the clinical judgment and review of the literature, including demographics, comorbidities, heart rate, systolic and diastolic blood pressure, HF-related symptoms, New York Heart Association (NYHA) classification, and laboratory tests. Based on previous literature, an MOR >1.2 indicates significant practice-level variation.6 We used the intraclass coefficient (ICC) to estimate the proportion of variance in spironolactone prescriptions that was attributable to between-hospital variations. We calculated the ICC from these hierarchical logistic models using the following equation: ICC = se²/(se² + (π²)/3), where se is the standard error of the random hospital intercept.14

To examine associations between hospital characteristics and rate of spironolactone prescription in the ideal and contraindicated patients at discharge, we divided hospitals into tertiles based on their respective rates (with the bottom tertile containing hospitals with the lowest rates and the top tertile containing hospitals with the highest rates). Within each rate tertile, a proportion was calculated for each categorical hospital characteristic and a median was calculated for each continuous hospital characteristic. To examine whether hospital

Yu et al  Hospital Variation of Spironolactone Use in HF

Statistical Analysis
We calculated the proportions of patients who received spironolactone prescriptions during hospitalization and at discharge among patients of different categories. We reported percentages to describe categorical variables and medians with interquartile ranges (IQRs) to describe continuous variables. We then compared patient characteristics by prescription of spironolactone in the ideal and contraindicated groups at discharge, respectively, using chi-square tests for categorical variables and Kruskal-Wallis test for continuous variables. Additionally, we compared the proportions of patients who received spironolactone prescriptions among ideal and contraindicated patients by hospital subtype.

To describe institutional-level variation in spironolactone prescriptions in the ideal and contraindicated groups at discharge, we assessed the median and IQR of spironolactone prescriptions. In this analysis, hospitals with <5 eligible patients for the group of interest (ideal or contraindicated) were excluded. We then used Spearman correlation to estimate the correlation in hospital-level spironolactone prescription between the ideal and contraindicated groups. To determine the effects of institutional variation in spironolactone prescriptions from the ideal and contraindicated groups, we used hierarchical logistic regression to calculate the median odds ratio (MOR). An MOR, eg, of 2.0, indicates that the odds of receiving a spironolactone prescription would be 2-fold higher for 2 patients with identical characteristics discharged from one random hospital versus another. Models were adjusted for patient characteristics and a random effect at the institutional level to account for the patients’ clustering within hospitals, with backward stepwise selection of covariates that were significant at the 0.05 level. We selected explanatory variables based on the clinical judgment and review of the literature, including demographics, comorbidities, heart rate, systolic and diastolic blood pressure, HF-related symptoms, New York Heart Association (NYHA) classification, and laboratory tests. Based on previous literature, an MOR >1.2 indicates significant practice-level variation.6 We used the intraclass coefficient (ICC) to estimate the proportion of variance in spironolactone prescriptions that was attributable to between-hospital variations. We calculated the ICC from these hierarchical logistic models using the following equation: ICC = se²/(se² + (π²)/3), where se is the standard error of the random hospital intercept.14

To examine associations between hospital characteristics and rate of spironolactone prescription in the ideal and contraindicated patients at discharge, we divided hospitals into tertiles based on their respective rates (with the bottom tertile containing hospitals with the lowest rates and the top tertile containing hospitals with the highest rates). Within each rate tertile, a proportion was calculated for each categorical hospital characteristic and a median was calculated for each continuous hospital characteristic. To examine whether hospital characteristics
characteristics differed across tertiles, continuous and categorical covariates at the hospital level were tested for trends using linear regression. To further determine which hospital characteristics were associated with the rate of spironolactone prescription, multivariable linear regression models with the respective rates as continuous outcome variables were performed. We reported percent change in respective rates with 95% CIs.

For all of the above explanatory variables, only NYHA classification and LVEF were missing in >1% of patients, and we created dummy variables as unrecorded/unmeasured. We imputed variables of missing rate <1% using median values. Statistical analysis was performed with SAS software version 9.3 (SAS Institute Inc.). All comparisons were 2-tailed, with P < 0.05 considered statistically significant.

RESULTS
Baseline Characteristics
Among 1222 ideal patients for spironolactone, 65.1% received spironolactone prescription at discharge (Figure 1). In the subgroup of 423 patients who were ideal for spironolactone and having both angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB) and β-blocker prescription at discharge, 88.2% received spironolactone. Among 900 patients with contraindications of spironolactone (serum creatinine >2.5 mg/dL in men or >2.0 mg/dL in women, or potassium >5.0 mEq/L, or documented allergy to spironolactone), 33.2% received spironolactone prescription at discharge. Spironolactone was prescribed to 39.7% (196/498) of patients with hyperkalemia, with 42.2% (171/405) and 26.9% (25/93) among patients with potassium 5 to 5.5 mmol/L and >5.5 mmol/L, respectively. Spironolactone was prescribed to 23.6% patients (117/495) with renal dysfunction. Among 7395 patients with uncertain benefit of spironolactone, 45.3% received spironolactone prescription at discharge. During hospitalization, the rate of spironolactone use among ideal and contraindicated patients were 88.4% (1099/1243) and 49.5% (517/1045), respectively. We compared patients who received a spironolactone prescription and those who did not among ideal and contraindicated patients at discharge, respectively (Tables S1 and S2).

Hospital Variation of Spironolactone Use
Among 189 hospitals that participated in the China PEACE 5r-HF study, 97 hospitals had at least 5 ideal patients and 83 hospitals had at least 5 contraindicated patients at discharge. The hospital-level spironolactone prescription rate in the ideal group ranged from 0% to 100% (median, 78.6%; IQR, 42.8%–89.6%); the hospital-level spironolactone prescription rate in the contraindicated group ranged from 0% to 100% (median, 30.0%; IQR, 9.1%–50.0%) (Figure 2). There was a positive correlation between spironolactone prescribed in the ideal and the contraindicated groups, with higher rates of prescription in the ideal group at institutions correlating with higher rates of prescription in the contraindicated group (Figure 3); the Spearman correlation coefficient was r=0.51 (P<0.001).

The MORs of spironolactone prescription for the ideal and the contraindicated were 3.4 (95% CI, 2.7–4.0) and 3.1 (95% CI, 2.4–3.9), respectively. Specifically, in the ideal group, 34% of the variance in spironolactone use was attributable to differences among hospitals (ICC=0.34), and 31% in the contraindicated group (ICC=0.31).
Hospital Characteristics Associated With Spironolactone Use

In stratified analysis of the prescription rate of spironolactone among ideal patients, hospitals in the top tertile had a higher proportion of teaching hospitals (82.3% versus 56.2%; \(P=0.035\)) and were more likely to have an independent department of cardiology (97.1% versus 68.7%; \(P<0.001\)) or were located in the Eastern (52.9% versus 21.9%;...
The prescription rate of spironolactone at discharge among ideal patients and contraindicated patients by hospital subtype are shown in Figures S1 and S2, respectively.

In stepwise linear regression, ideal patients treated in hospitals with an independent department of cardiology had a 38.0% (95% CI, 18.7–57.3; \( P<0.001 \)) higher of rate to receive spironolactone than in hospitals without an independent department of cardiology (Table 3). Similarly, Eastern hospitals had a mean rate that was 14.6% (95% CI, 2.3%–26.9%; \( P=0.020 \)) higher than that of hospitals in the Western and Central regions. None of the collected hospital characteristics were significantly associated with the spironolactone use in the contraindicated patients.

**DISCUSSION**

In this hospital-level assessment of a national cohort of patients hospitalized for HF in China, we found that 1 in 4 patients who were ideal candidates for spironolactone therapy were not treated and almost 1 in 3 with a contraindication to spironolactone were treated. A positive correlation between hospital-level use in the ideal and the contraindicated groups was identified. Underuse and inappropriate use varied markedly by hospital. Hospitals with an independent department of cardiology and those located in the Eastern region were more likely to prescribe spironolactone in ideal patients. These findings indicate targets for quality improvement of HF care.

To our knowledge, this is the first study to assess the appropriateness of spironolactone use in China.
We found 78.6% of patients with LVEF ≤40% received a spironolactone prescription at discharge; the rate reached almost 90% when further limited to patients who were already taking an ACEI and β-blocker. This result was in accordance with previous findings and extended by using a national representative sample of HF admissions. Although the rate of spironolactone use in ideal patients was much higher in China compared with in the United States, Europe, and Korea, where the rates ranged from 30% to 50%, there is still room for improvement. By contrast, we found opposite practice patterns for the use of ACEIs/angiotensin receptor blockers or β-blockers among the ideal patients with HF, whose use rates are much lower in China than those in western countries (about 50% versus nearly 90%). Since ACEIs are substantially underused despite being inexpensive, the wide adoption of spironolactone in China cannot be explained solely

| Table 1. Hospital Characteristics Across Tertiles of Prescription Rate of Spironolactone Among Ideal Patients |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                                | Overall (N=97)  | T1 (n=32)       | T2 (n=31)       | T3 (n=34)       | P value          |
| Prescription rate of spironolactone, % | (0–100)         | (0–58.3)        | (58.3–85.7)     | (85.7–100)      |
| Hospital level, n (%)          |                 |                 |                 |                 | 0.619            |
| Tertiary                       | 47 (48.4)       | 15 (46.9)       | 14 (45.2)       | 18 (52.9)       |
| Location, n (%)                |                 |                 |                 |                 | 0.034            |
| Eastern                        | 37 (38.1)       | 7 (21.9)        | 12 (38.7)       | 18 (52.9)       |
| Central                        | 24 (24.7)       | 11 (34.4)       | 7 (22.6)        | 6 (17.6)        |
| Region, n (%)                  |                 |                 |                 |                 | 0.796            |
| Urban                          | 46 (47.4)       | 14 (43.7)       | 16 (51.6)       | 16 (47.1)       |
| Teaching hospital, n (%)       | 65 (67.0)       | 18 (56.2)       | 19 (61.3)       | 28 (82.3)       |
| Medical university–affiliated hospital, n (%) | 34 (35.0)       | 9 (28.1)        | 10 (32.3)       | 15 (44.1)       |
| Catheterization laboratory, n (%) | 63 (64.9)     | 18 (56.2)       | 20 (64.5)       | 25 (73.5)       |
| No. of beds, median, IQR       | 829 (360–1600)  | 799 (260–1448)  | 798 (360–1300)  | 1200 (560–1648) |
| Capacity of CABG, n (%)        | 33 (34.0)       | 9 (28.1)        | 10 (32.3)       | 14 (41.2)       |
| Independent department of cardiology, n (%) | 84 (86.6)       | 22 (68.7)       | 29 (93.5)       | 33 (97.1)       |
| **P value**                    |                 |                 |                 |                 |                  |

CABG indicates coronary artery bypass graft; and IQR, interquartile range.

| Table 2. Hospital Characteristics Across Tertiles of Prescription Rate of Spironolactone Among Contraindicated Patients |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                                | Overall (N=83)  | T1 (n=29)       | T2 (n=28)       | T3 (n=26)       | P value          |
| Prescription rate of spironolactone, % | (0–100)         | (0–16.7)        | (16.7–40.0)     | (40.0–100)      |
| Hospital level, n (%)          |                 |                 |                 |                 | 0.486            |
| Tertiary                       | 39 (47.0)       | 15 (51.7)       | 13 (46.4)       | 11 (42.3)       |
| Location, n (%)                |                 |                 |                 |                 | 0.684            |
| Eastern                        | 38 (45.8)       | 9 (31.0)        | 17 (60.7)       | 12 (46.1)       |
| Central                        | 22 (26.5)       | 13 (44.8)       | 3 (10.7)        | 6 (23.1)        |
| Region, n (%)                  |                 |                 |                 |                 | 0.317            |
| Urban                          | 47 (66.6)       | 15 (51.7)       | 15 (53.6)       | 17 (65.4)       |
| Teaching hospital, n (%)       | 57 (68.7)       | 20 (69.0)       | 19 (67.9)       | 18 (69.2)       |
| Medical university–affiliated hospital, n (%) | 28 (33.7)       | 11 (37.9)       | 11 (39.3)       | 6 (23.1)        |
| Catheterization laboratory, n (%) | 53 (63.9)     | 19 (65.5)       | 17 (60.7)       | 17 (65.4)       |
| No. of beds, median, IQR       | 700 (344–1300)  | 850 (330–1600)  | 605 (352–1230)  | 700 (365–1200)  |
| Capacity of CABG, n (%)        | 22 (26.5)       | 8 (27.6)        | 8 (28.6)        | 6 (23.1)        |
| Independent department of cardiology, n (%) | 71 (85.5)       | 25 (86.2)       | 24 (85.7)       | 22 (84.6)       |
| **P value**                    |                 |                 |                 |                 | 0.258            |

CABG indicates coronary artery bypass graft; and IQR, interquartile range.
by its low price. The underlying reasons are unknown but may result from the diuretic effect of spironolactone and the desire to use a potassium-sparing agent.

Despite the encouraging use of spironolactone in the ideal candidate, the wide use of spironolactone among individuals with contraindications is concerning and likely undermines the population-level benefit of this agent in the population with HF. Despite the clear benefits of spironolactone in select patients who have HF with reduced ejection fraction, inappropriate use can expose patients to potential harm, including worsening hyperkalemia or significant renal dysfunction or even death. A previous study found that spironolactone use significantly increased to ≈28% in contraindicated patients with acute myocardial infarction in China during 2001 to 2011. We found that the inappropriate use rate was slightly higher in contraindicated patients with HF in 2015. Specifically, the United States had experienced increased inappropriate use of spironolactone to ≈30% among patients with LVEF <40% after RALES (Randomized Aldactone Evaluation Study), which demonstrated the benefit of AAs for HF. However, after several publications showed excess adverse events associated with inappropriate use, the rate soon witnessed a declining trend to ≈10%. This suggests that physicians’ understanding about the benefit and risk is important for medicine use. Notably, spironolactone was prescribed to 2 in 5 patients with hyperkalemia at discharge. Perhaps the hyperkalemia was caused by the inpatient spironolactone use or other reasons and the therapy was not suspended at discharge. Substantial efforts are needed to improve the appropriateness of spironolactone use across China, including spreading knowledge about the potential harm of inappropriate use and surveillance of adverse events attributable to inappropriate use.

The current study bridges a knowledge gap with two important findings in the hospital-level use of spironolactone. First, we demonstrated substantial hospital-level variation in spironolactone prescription for both the ideal and the contraindicated candidates. Similar institution-level variation was also observed for the use of ACEIs/angiotensin receptor blockers and β-blockers among ideal patients with HF. Second, higher use in patients who would benefit is correlated with higher use in those who might be harmed. At the population level, this could be translated into a minimal net benefit in real-world practice patterns. Considering the relatively higher use of spironolactone in China, more attempts are needed to emphasize the careful selection of patients and avoid potentially harmful use. The Chinese Hospital Association has created a single disease quality management project including prescription of AAs among indicated patients as one of the targets for quality improvement of HF care at the hospital level since 2009. Further efforts are needed to monitor the use of AAs at the hospital level.

We provide new information about hospital characteristics associated with spironolactone use. Hospitals with independent cardiology departments and those in the Eastern region of China were associated with better adherence to evidence-based spironolactone use. This finding signifies the importance of superior access to knowledge and health care resources. These findings are consistent with the survey on knowledge of HF guidelines among 2146 clinicians from 88 hospitals in China, which reported that more than two-thirds of physicians failed to fully obtain the indications and contraindications of spironolactone, and general practitioners had poorer awareness of HF guidelines than cardiovascular specialists. The findings indicate the need for further training of clinicians to improve their knowledge and practice related to guideline-recommended spironolactone prescription.

Our study should be interpreted in the context of several limitations. First, LVEF was not assessed in about a third of the patients; given this condition, we may have excluded some patients who would be considered ideal candidates. However, the physicians also determined whether to use spironolactone without considering ideal candidates. However, the physicians also determined whether to use spironolactone without having LVEF information available. Second, only about half of the hospitals had enough candidates for the hospital-level analysis. However, current assessment includes hospitals from all economic–geographical regions and hospitals of different levels, which justifies the current analysis in representing the practice patterns. Third, we may have underestimated the ideal group as spironolactone is also indicated in other diseases except for HF. Fourth, we cannot analyze the dose of spironolactone as this variable was missing.

In conclusion, we identified the opportunities of optimizing the use of spironolactone among HF admissions, including raising utilization among ideal patients and lowering inappropriate utilization among contraindicated patients. Significant hospital-level variation in spironolactone use among contraindicated and ideal patients suggests the importance of systematic factors in spironolactone prescribing. Further efforts in
illuminating the barriers to more-appropriate use of evidence-based therapies, as well as identifying the local barriers to spironolactone prescription, will be needed to maximize the benefit and minimize the potential harm in utilizing spironolactone among patients with HF.

ARTICLE INFORMATION
Received April 5, 2022; accepted August 25, 2022.

Affiliations
National Clinical Research Center of Cardiovascular Diseases, National Health Commission Key Laboratory of Clinical Research for Cardiovascular Medications, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, People’s Republic of China (Y.Y., W.G., B.W., G.H., J.L.); Ascension Health, St Louis, MO (F.A.M.); Division of Cardiology, University of Colorado Anschutz Medical Campus, Aurora, CO (F.A.M.); School of Medicine, University of Missouri, Kansas City, MO (J.A.S.); Saint Luke’s Mid America Heart Institute, Kansas City, MO (J.A.S.); Center for Outcomes Research and Evaluation, Yale-New Haven Hospital, and Department of Internal Medicine, Yale University School of Medicine, New Haven, CT (H.M.K.); Center for Outcomes Research and Evaluation, Yale-Figueroa Hospital, New Haven, CT (H.M.K.); Department of Health Policy and Management, Yale School of Public Health, New Haven, CT (H.M.K.); Section of Cardiovascular Medicine, Department of Internal Medicine, Yale School of Medicine, New Haven, CT (H.M.K.); and Wuhan hospital, Chinese Academy of Medical Sciences, Shenzhen, P. R. China (J.L.).

Acknowledgments
We appreciate the multiple contributions made by project teams at the China National Clinical Research Center of Cardiovascular Diseases and Yale-New Haven Hospital Centers for Outcomes Research and Evaluation in the realms of study design and operations. The site investigators are listed in Data S1. We appreciate Xiaofang Yan, MS; Yuyue Xi, MS; Jiangling Liu, BS; Linda Sun, BS; Yuanyuan Luo, MD; and Jianmin Liu, MD, PhD; for their contributions to data collection; Wuhanbilei Hundei, MD, for his contributions to data quality control; Hongzhao Zhang, MPH; Jiali Song, MD; Wenbo Zhang, MS; Weihong Guo, MD; and Teng Li, MD; for their contributions to data cleaning.

Sources of Funding
This work was supported by the China Academy of Chinese Medical Sciences Innovation Fund for Medical Science (2021-I2M-1-009), the National Key Technology R&D Program (2015BAI12B02) from the Ministry of Science and Technology of China and the 111 Project from the Ministry of Education of China (B16005).

Disclosures
Dr Li reported receiving research grants, through Fuwai hospital, from Chinese government and Chinese Academy of Medical Sciences for work to improve the management of hypertension and blood lipids and to improve patient outcomes of cardiovascular disease and COVID-19; receiving research agreements, through the National Center for Cardiovascular Diseases and Fuwai Hospital, from Amgen for a multicenter clinical trial assessing the efficacy and safety of omecamtiv mecarbil and for dyslipidemic patient registration; receiving a research agreement, through Fuwai Hospital, from Sanofi for a multicenter clinical trial on the effects of sotagliflozin; receiving a research agreement, through Fuwai Hospital, with the University of Oxford for a multicenter clinical trial of empagliflozin; receiving a research agreement, through the National Center for Cardiovascular Diseases, from AstraZeneca for clinical research methods training outside the submitted work; and receiving a research agreement, through the National Center for Cardiovascular Diseases, from Lilly for physician training outside the submitted work. In the past 3 years, Dr Krumholz received expenses and/or personal fees from UnitedHealth; Element Science, Aetna, Reality Labs, the Siegfried and Jensen Law Firm, Arnold and Porter Law Firm, Martin/ Baugham Law Firm, and F-Prime. He is a co-founder of Refactor Health and HugoHealth and is associated with contracts, through Yale New Haven Hospital, from the Centers for Medicare & Medicaid Services and through Yale University from Johnson & Johnson. Dr Masoudi has a contract with the American College of Cardiology for his role as Chief Science Officer of the NCDR. Dr Spertus is the principal investigator of grants from the National Institutes of Health, Abbott Vascular, Janssen, Myocardia and the American College of Cardiology Foundation; is a consultant for Janssen, Novartis, Amgen, Myokardia, AstraZeneca, Bayer and Merck; serves on the scientific advisory board of UnitedHealthcare and the Board of Directors for Blue Cross Blue Shield of Kansas City; and owns the copyright to the Kansas City Cardiomyopathy Questionnaire, Seattle Angina Questionnaire, and Peripheral Artery Questionnaire. No other disclosures were reported.

Supplemental Material
Appendix S1

REFERENCES
1. Heart Failure Group of Chinese Society of Cardiology of Chinese Medical Association; Chinese Heart Failure Association of Chinese Medical Doctor Association; Editorial Board of Chinese Journal of Cardiology. [Chinese guidelines for the diagnosis and treatment of heart failure 2018]. Zhonghua Xin Xue Guan Bing Za Zhi. 2018 Oct 24;46(10):760–789. Chinese. doi: 10.3760/cma.j.issn.0253-3758.2018.10.004
2. Writing Committee Members, Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, Foranov GC, Geraci SA, Horwich T, Januzzi JL, American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines. Circulation. 2013;128:e240–e327. doi: 10.1161/CIR.0b013e31829e8776
3. Zannad F, McMurray JJ, Krum H, van Veldhuisen DJ, Swedberg K, Shi H, Vincent J, Pocock SJ, Pitt B, EMPHASIS-HF Study Group. Eplerenone in patients with systolic heart failure and mild symptoms. N Engl J Med. 2011;364:11–21. doi: 10.1056/NEJMoa1009492
4. Pitt B, Zannad F, Remme WJ, Cody R, Casteigne A, Perez A, Palensky J, Wittes J. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone evaluation study investigators. N Engl J Med. 1999;341:709–717. doi: 10.1056/NEJM199909233411001
5. Tamirisa KP, Aaronson KD, Koelling TM. Spironolactone-induced renal insufficiency and hyperkalemia in patients with heart failure. Am J Heart J. 2004;148:971–978. doi: 10.1016/j.ajh.2004.10.005
6. Dev S, Lacy ME, Masoudi FA, Wu WC. Temporal trends and hospital variation in mineralocorticoid receptor antagonist use in veterans discharged with heart failure. J Am Heart Assoc. 2015;4:e002268. doi: 10.1161/JAHA.115.002268
7. Albert NM, Yancy CW, Jiang L, Zhao X, Hernandez AF, Peterson ED, Cannon CP, Foranov GC. Use of aldosterone antagonists in heart failure. JAMA. 2009;302:1658–1665. doi: 10.1001/jama.2009.1493
8. Curtis LH, Mi X, Qualls LG, Check DK, Hammill BG, Hammill SC, Heidenreich PA, Masoudi FA, Setoguchi S, Hernandez AF, et al. Translational adherence and persistence in the use of aldosterone antagonist therapy in patients with heart failure. Am Heart J. 2013;165:979–986.e10. doi: 10.1016/j.jahj.2015.03.007
9. Gupta A, Yu Y, Tan Q, Liu S, Masoudi FA, Du X, Zhang J, Krumholz HM, Li J. Quality of care for patients hospitalized for heart failure in China. JAMA Netw Open. 2020;3:e1918619. doi: 10.1001/jamanetworkopen.2019.18619
10. Zhang Y, Zhang J, Butler J, Yang X, Xie P, Guo D, Wei T, Yu J, Wu Z, Gao X, et al. Contemporary epidemiology, management, and outcomes of patients hospitalized for heart failure in China: Results from the China heart failure (China-HF) registry. J Card Fail. 2017;23:868–875. doi: 10.1016/j.cardfail.2017.09.014
11. Liu X, Yu H, Pei J, Chu J, Pu J, Zhang S. Clinical characteristics and long-term prognosis in patients with chronic heart failure and reduced ejection fraction in China. Heart Lung Circ. 2014;23:818–826. doi: 10.1016/j.hlc.2014.02.022
12. Yu Y, Gupta A, Wu C, Masoudi FA, Du X, Zhang J, Krumholz HM, Li J. Characteristics, management, and outcomes of patients hospitalized for heart failure in China: The China PEACE retrospective heart failure study. J Am Heart Assoc. 2019;8:e012884. doi: 10.1161/JAHA.119.012884
13. Yu Y, Zhang H, Li X, Lu Y, Masoudi FA, Krumholz HM, Li J. The China patient-centered evaluative assessment of cardiac events.
[China PEACE] retrospective heart failure study design. BMJ Open. 2018;8:e020918.

14. Merlo J, Chaix B, Olisson H, Beckman A, Johnell K, Hjerpe P, Rastam L, Larsen K. A brief conceptual tutorial of multilevel analysis in social epidemiology: Using measures of clustering in multilevel logistic regression to investigate contextual phenomena. J Epidemiol Community Health. 2006;60:290–297. doi: 10.1136/jech.2004.029454

15. He L, Dong J, Du X, Jiang C, Chen N, Xia SJ, Hou XX, Yu HR, Lv Q, Yu RH, et al. Healthcare quality and mortality among patients hospitalized for heart failure by hospital level in Beijing, China. ESC heart failure. 2021;8:1186–1194. doi: 10.1002/ehf2.13178

16. Komajda M, Hanon O, Hochadel M, Lopez-Sendon JL, Follath F, Ponikowski P, Harjola VP, Dickstein K, Tavazzi L, et al. Contemporary management of octogenarians hospitalized for heart failure in Europe: Euro heart failure survey II. Eur Heart J. 2009;30:478–486. doi: 10.1093/eurheartj/ehn539

17. Youn YJ, Yoo BS, Lee JW, Kim JY, Han SW, Jeon ES, Cho MC, Kim JJ, Kang SM, Chae SC, et al. Treatment performance measures affect clinical outcomes in patients with acute systolic heart failure: Report from the Korean heart failure registry. Circulation J. 2012;76:1151–1158. doi: 10.1253/circj.CJ-11-1093

18. Writing Group Members, Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, Das SR, de Ferranti S, Despres JP, Fullerton HJ, American Heart Association Statistics Committee; Stroke Statistics Subcommittee, et al. Heart disease and stroke statistics-2016 update: A report from the American Heart Association. Circulation. 2016;133:e38–e360. doi: 10.1161/CIR.0000000000000350

19. Nieminen MS, Brutsaert D, Dickstein K, Drexler H, Follath F, Harjola VP, Hochadel M, Komajda M, Lassus J, Lopez-Sendon JL, et al. EuroHeart failure survey II (EHFS II): A survey on hospitalized acute heart failure patients: Description of population. Eur Heart J. 2006;27:2725–2736. doi: 10.1093/eurheartj/ehl193

20. Tseng WC, Liu JS, Hung SC, Kuo KL, Chen YH, Tang DC, Hsu CC. Effect of spironolactone on the risks of mortality and hospitalization for heart failure in pre-dialysis advanced chronic kidney disease: A nationwide population-based study. Int J Cardiol. 2017;238:72–78. doi: 10.1016/j.ijcard.2017.03.080

21. Guan W, Murugiah K, Downing N, Li J, Wang Q, Ross JS, Desai NR, Masoudi FA, Spertus JA, Li X, et al. National quality assessment evaluating spironolactone use during hospitalization for acute myocardial infarction (AMI) in China: China patient-centered evaluation assessment of cardiac events (PEACE)-retrospective AMI study, 2001, 2006, and 2011. J Am Heart Assoc. 2015;4:e001718. doi: 10.1161/JAHA.114.001718

22. Masoudi FA, Gross CP, Wang Y, Rathore SS, Havranek EP, Foody JM, Krumholz HM. Adoption of spironolactone therapy for older patients with heart failure and left ventricular systolic dysfunction in the United States, 1998–2001. Circulation. 2005;112:39–47. doi: 10.1161/CIRCULATIONAHA.104.527549

23. Bozkurt B, Agoiston I, Knowlton AA. Complications of inappropriate use of spironolactone in heart failure: When an old medicine spirals out of new guidelines. J Am Coll Cardiol. 2003;41:211–214. doi: 10.1016/S0735-1097(02)02694-3

24. Ministry of Health of the People’s Republic of China. The quality-control indicators for single disease (version 2009). 2009;2017.

25. Gan TY, Liu NN, Zhang YH, Lv R, Zhao XM, Huang YH, Zhang J. A knowledge survey on heart failure guidelines in physicians. Chinese Circulation Journal. 2017;32:952–955.
SUPPLEMENTAL MATERIAL
Data S1. China PEACE 5r-HF Study site investigators by hospital

Anhui Province, Dingyuan County General Hospital, Xinning Ma, Wenhua Zhang; Huangshan Third People's Hospital, Changjie Hong, Fang Wang; Bengcheng County First People's Hospital, Gaofeng Guo; Beijing, Peking University People's Hospital, Hong Chen, Huiping Li, Yu Luo; Beijing Watson Hospital, Lihua Shang, Jing Wang, Xinhua Xu; Yanqing District Hospital of Beijing, Li Yang, Xiaolei He; Chongqing, Tongliang County People's Hospital, Guofu Li; Chongqing Sixth People's Hospital, Yonghong Huang; Fuling Central Hospital of Chongqing, Liquan Xiang, Lin Ning, Peng Xiao; Nanchuan District People's Hospital of Chongqing, Lingxian Zeng; Fujian Province, Fujian Provincial Hospital, Yansong Guo, Lirong Lin; Longyan City, Fujian Province First Hospital, Haiming Yi, Kaihong Chen, Yong Lin; Wuyishan City, Fujian Province Hospital, Qingfei Lin, Chuxia Liu; Fuzhou First Affiliated Hospital of Fujian Medical University, Yan Zhang, Yu Ouyang, Chuanchuan Li; Nanan Hospital, Duanping Dai, Shaoxiong Hong; Zhoushan County Hospital, Banghua He, Miaoli Huang; Gansu Province, Minxian County People's Hospital of Gansu Province, Yuhong Liu, Minwu Bao, Hongliang Chu; Jiuquan City People's Hospital, Yaofeng Yuan, Zhirong Li; Hongzhou District, Lanzhou City People's Hospital, Ping Zhang; Sunan Yugur Autonomous County People's Hospital, Zhanzheng Ba, Wanhai Fu; Zhangjiachuan Hui Autonomous County People's Hospital, Shitang Gao, Qiang Gao; Guangdong Province, Peking University Shenzhen Hospital, Chun Wu, Huan Qu, Yinhong Du; Panyu District, Guangzhou City Central Hospital, Guoqin Chen, Jinliang Li; Huizhou City People's Hospital, Yuansheng Bai, Jie Li; Guangxi Province, Fengshan County People's Hospital, Wen Long, Shilin Lu, Jianhua Huang; Gongcheng Yao Autonomous County People's Hospital, Mingfeng Feng, Mao Rong; Guilin People's Hospital, Diguang Pan, Weihua Tang, Yi Ding; Guiping City People's Hospital, Guang Chen, Yongxian Rong; Jingxi County People's Hospital, Wei Jiang, Chen Yuan; Rongjiang County People's Hospital, Fangning Wang; Shouguang Shuicheng Iron and Steel (Group) Co., Ltd. General Hospital, Min Zhang, Lala Li; Hainan Province, Hainan West Central Hospital, Zhongwei Wu; Hainan Medical College Hospital, Yueqiong Kong, Yang Yang; Hebei Province, Baoding Second Central Hospital, Guan Ma, Jing Zhao; Second Affiliated Hospital of Hebei North University, Wenhui Li, Peitian Han; First Affiliated Hospital of Hebei North University, Fangjiang Li, Aiai Zhang, Feixing Li; Jize County Hospital, Qiu'e Guo, Han Cui, Ruizhong Li; Jingxing Hospital, Zhenhai Zhao, Jun Yin; Kangbao County People's Hospital, Ruizhong Zhao, Guangjun Song; Laoting County Hospital, Keyong Shang; Shijiazhuang City Luan City People's Hospital, Ruigang Zhao, Tao Jia; Kaiping Hospital of Tangshan City, Yanmin Yao, Yaoqi Liu; Wuqing County People's Hospital, Binglu Liu, Hongguang Zang; Henan Province, First Affiliated Hospital of Henan University of Science and Technology, Pingshuan Dong, Xuming Yang, Laijing Du; Henan Provincial People's Hospital, Chuanyu Gao, Xinyun Liu; Kaifeng Integrative Medicine Hospital, Lei Qin, Jieyun Liu, Xiaoxin Wang; Luyi County People's
Hospital, Rui Xiao, Xiaoming Gang; Anshan Mayor Hospital, Xiang Jin, Ting Cai; Beipiao Central Hospital, Han Yu, Congwei Huo, Wei Feng; Changtu County First Hospital, Mingbao Sun, Wei Zhang; Zhongshan Hospital Affiliated to Dalian University, Qin Yu, Qianru Bai; Dalian Fifth General Hospital, Haiyan Shao, Jing Zhang; Dalian Central Hospital, Yongchao Zhi, Lili Sun; Dashiqiao Central Hospital, Juan Huang, Qiang Zhang; Liaoayang City Central Hospital, Yingying Li; Yuhong District, Shenyang City People's Hospital, Meijuan Piao, Lili Xin; Inner Mongolia, Alxa League Hospital, Shiguo Hao, Xiaoao Liu; Baotou Fourth Hospital, Baohong Zhang, Conghong Shi; Hellinger County People's Hospital, Yongshuan Wu, Qiuli Wang, Zhiqiang Sun; Keshiketeng Banner Hospital, Lize Wang, Chen Yan, Jian Chen; Hohhot, Hohhot Saihan District Second People's Hospital, Rongjuan Zhang; Inner Mongolia Siziwangqi People's Hospital, Hongtu Zhang, ShuJiang Wang; Tongliao City Horqin District First People's Hospital, Junping Fang, Xinli Yu; Wuhai People's Hospital, Zhaohai Zhou, Lei Shi; Wulatetqianqi People's Hospital, Jinlan Xu, Dandan Wang; Wulanchabu City Central Hospital, Dajun Liu, Xinhong Cao; Zuozi County People's Hospital, Julong Hao, Chunwang Ren; Ningxia, Guyuan Yuanzhou District People's Hospital, Xiaoping Gao, Lining You; Qinghai Province, Qinghai Red Cross Hospital, Yanmei Shen, Xiao Hu; Qinghai Province Fifth People's Hospital, Hong Wu; Zaduo County People's Hospital of Qinghai Province, Cairen Nima, Wangzha Chenglin; Xining Third People's Hospital, Qing Feng, Jiao Wang; Xinghai County People's Hospital, Guohui Zhou; Shandong Province, Heze City Hospital, Wentang Niu, Sixia Feng; Jining City People's Hospital, Chuanxin Li, Binbao Xiao; Heze City, Shandong Province Chengwu County People's Hospital, Fengqin Liu, Lijuan Wang; Shanxi Province, Huaioren County People's Hospital, Ling Tong; Ningwu County People's Hospital, Junhu An; Qinshui County People's Hospital, Hehua Zhang, Yong Gao; Lucheng People's Hospital of Shanxi Province, Yunke Zhou, Xiaoxia Niu; Pianguan County People's Hospital of Shanxi Province, Jinsong Jiao; Xing County, Shanxi Province People's Hospital, Aiping Lv, Yan Zhao; Yuncheng City, Shanxi Province Central Hospital, Bo Wang, Yingjia Li, Zhuoxxuan Yang; Zuo Yun County People's Hospital of Shanxi Province, Ru Duan, Xiaolin Li; Taiyuan Xinghualing District Central Hospital, Yueli Qu, Zhimei Yang, Xiaoming Wei; Yanggao County People's Hospital, Zhiru Peng, Yan Han, Hongxia Zhang; Ying County People's Hospital, Wenbing Zhao; Shaanxi Province, Fugu County People's Hospital, Ruijun Hao; Huayin City People's Hospital, Aiping Wang, Feipeng Li; Tongchuan Mining Central Hospital, Guojiong Jia, Huiping Yang; Xi'an First Hospital, Yuqiang Ji, Xia Li; Yangling Demonstration Area Hospital, Xueqiang Yang, Honglei Zhang; Shanghai, Shanghai Jiao Tong University School of Medicine Ruijin Hospital, Xiaoxiang Yan; Sichuan Province, Aba Tibetan and Qiang Autonomous Prefecture People's Hospital, Bo Cai, Fangan Li; Guangyuan First People's Hospital, Tianxun Wang, Xiaoying Wang; Muli Tibetan Autonomous County People's Hospital, Hui Peng; Daofu County People's Hospital of Sichuan Province, Jiekang Liu, Lamu Nima; Guan'an Huayang City People's Hospital of Sichuan Province, Zhihong Zhang; Xuanhan County People's Hospital, Xuan Ma, Guochun Jin; Fourth People's Hospital of Zigong City, Yong Yi; Tianjin, Tianjin Jinghai County Hospital, Yuling Zhang, Yan Hua; Tianjin Medical University General Hospital, Yuelin Sun, Bo Bian; Tibet, Gyantse People's Hospital, OuZhu Danzeng, Ge Sang, Pu Pian; Xinjiang, Bortala Mongol Autonomous Prefecture People's Hospital, Ping Chen, Edina Cullens; Yunnan Province, Gongshan Dulong Nu Autonomous County People's Hospital, Xiaoping Wu, Yanmin He; Jinning County People's Hospital, Lihua Gu; Lanping Bai Minority Autonomous
County People's Hospital, Runxiang He, Jinwen He; Menglian Dai Lahu and Wa Autonomous County People's Hospital, Xiang Li; Qujing Qilin District People's Hospital, Fuyong Li, Yingshuang Yuan, Yuchun Zhang; Yunlong County People's Hospital, Jianxun Yang, Song Ai, Baolong Wang; Zhejiang Province, Dongyang City People's Hospital, Liang Lu, Tingying Xu; Haiyan County People's Hospital, Chunhui Xiao, Zhihua Lu; Huzhou Nanxun People's Hospital, Weili Jin, Fuqin Zhu; Jiaxing Nanhu District Central Hospital East New Campus, Zhihua Sun; Yueqing People's Hospital, Xudong Yu, Qiu Wang; Quzhou City People's Hospital, Xiaoming Tu; Shengsi People's Hospital, Songguo Wang; Taizhou Hospital of Zhejiang Province, Yafei Mi, Weiwei Zhou, Jianjun Jiang; Wencheng County People's Hospital of Zhejiang Province, Junlu Wang, Haisheng Zhu; Yuyao City, Zhejiang Province People's Hospital, Lailin Deng, Lian Chen.
### Table S1. Patient characteristics by spironolactone prescription at discharge among ideal patients with HF

|                                | Overall (n=1222) | Spironolactone prescription | P     |
|--------------------------------|------------------|----------------------------|-------|
|                                |                  | Yes (n=795) | No (n=427) |
| **Social demographic**         |                  |              |            |
| Age (years), median, IQR       | 68 (59, 75)      | 68 (60, 75) | 67 (58, 76) | 0.211 |
| Female (%)                     | 36.2             | 35.1         | 38.2        | 0.286 |
| **Comorbidities (%)**          |                  |              |            |
| Prior myocardial infarction    | 17.5             | 18.7         | 15.2        | 0.123 |
| Coronary artery disease        | 62.0             | 62.6         | 60.7        | 0.495 |
| Hypertension                   | 43.1             | 45.2         | 39.3        | 0.050 |
| Atrial fibrillation            | 27.7             | 27.6         | 28.1        | 0.836 |
| Cardiac valvular disease       | 64.2             | 64.2         | 64.2        | 0.995 |
| Dyslipidemia                   | 61.2             | 64.0         | 56.0        | 0.006 |
| Stroke/transient ischemic attack| 14.2             | 14.1         | 14.3        | 0.925 |
| Diabetes mellitus              | 19.9             | 20.1         | 19.4        | 0.774 |
| Chronic renal insufficiency    | 12.8             | 13.6         | 11.2        | 0.242 |
| Peripheral arterial disease    | 8.5              | 10.4         | 4.9         | 0.001 |
| COPD or asthma                 | 21.0             | 18.9         | 25.1        | 0.011 |
| **Clinical presentation at**   |                  |              |            |
| discharge                                      | 7.1 | 8.3 | 4.9 | 0.009 |
|------------------------------------------------|-----|-----|-----|-------|
| Jugular vein distension (%)                    |     |     |     |       |
| Pulmonary rales present (%)                    | 14.0| 14.2| 13.6| 0.762 |
| Lower extremity edema (%)                      | 6.1 | 5.9 | 6.6 | 0.654 |
| Heart rate (beats/min)                         | 75 (70, 80) | 75 (70, 80) | 76 (70, 82) | 0.058 |
| Systolic blood pressure (mmHg)                 | 120 (110, 130) | 120 (109, 128) | 120 (110, 130) | 0.297 |
| NYHA functional class (%)                      |     |     |     | 0.275 |
| I-II                                           | 6.8 | 6.9 | 6.6 |       |
| III                                            | 40.0| 40.2| 39.6|       |
| IV                                             | 46.2| 46.9| 45.0|       |
| Unrecorded                                     | 7.0 | 5.9 | 8.9 |       |

**Discharge lab value**

| Potassium, mEq/L, median, IQR                  | 4.1 (3.7, 4.4) | 4.0 (3.7, 4.4) | 4.2 (3.8, 4.4) | 0.004 |
| Serum creatine, mg/dL, median, IQR            | 1.0 (0.8, 1.2) | 1.0 (0.8, 1.2) | 1.0 (0.8, 1.2) | 0.786 |

**Echocardiography**

| LVEF                                           | 32 (27, 36) | 32 (27, 36) | 32 (27, 36) | 0.761 |

**Medications at discharge (%)**

| ACEI or ARB                                    | 51.1 | 67.3 | 20.8 | <0.001 |
|                       |        |        |      |      |
|-----------------------|--------|--------|------|------|
| **β blocker**         | 46.8   | 61.8   | 19.0 | <0.001 |
| Loop diuretics        | 52.0   | 74.7   | 9.6  | <0.001 |
| Thiazide diuretics    | 11.9   | 16.1   | 4.0  | <0.001 |

NYHA indicates New York Heart Association; LVEF, left ventricular ejection fraction; ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker
Table S2. Patient characteristics by spironolactone prescription at discharge among contraindicated patients with HF

| Social demographic | Overall (n=900) | Spironolactone prescription | P      |
|--------------------|----------------|-----------------------------|--------|
|                    |                | Yes (n=299) | No (n=601) |        |
| Age (years), median, IQR | 72 (63, 79) | 74 (64, 80) | 71 (62, 79) | 0.025  |
| Female (%)         | 50.2           | 58.5            | 46.1            | <0.001 |

| Comorbidities (%) |                    |                |       |
|-------------------|-------------------|----------------|------|
| Prior myocardial infarction | 8.8           | 9.0            | 8.6  | 0.850 |
| Coronary artery disease   | 56.2           | 56.5           | 56.1 | 0.898 |
| Hypertension         | 66.2           | 58.2           | 70.2 | <0.001|
| Atrial fibrillation  | 30.6           | 41.5           | 25.1 | <0.001|
| Cardiac valvular disease | 31.7           | 41.8           | 26.6 | <0.001|
| Dyslipidemia         | 51.1           | 47.8           | 52.7 | 0.164 |
| Stroke/transient ischemic attack | 17.9       | 17.7           | 18.0 | 0.928 |
| Diabetes mellitus   | 29.3           | 20.4           | 33.8 | <0.001|
| Chronic renal insufficiency | 61.4       | 46.5           | 68.9 | <0.001|
| Peripheral arterial disease | 8.3        | 12.4           | 6.3  | 0.002 |
| COPD or asthma      | 24.8           | 20.4           | 27.0 | 0.032 |

Clinical presentation at
### discharge

|                          |    |    |    |     |
|--------------------------|----|----|----|-----|
| Jugular vein distension (%) | 8.2| 0.7| 7.0| 0.122 |
| Pulmonary rales present (%) | 20.1| 18.4| 21.0| 0.365 |
| Lower extremity edema (%)   | 14.3| 12.4| 15.3| 0.237 |
| Heart rate (beats/min)      | 76 (70, 84) | 76 (70, 82) | 76 (70, 85) | 0.435 |
| Systolic blood pressure (mmHg) | 125 (113, 140) | 120 (110, 130) | 130 (118, 140) | <0.001 |
| NYHA functional class (%)   |  |    |    | <0.001 |
| I-II                      | 8.8| 8.4| 9.0| |
| III                       | 34.9| 36.8| 33.9| |
| IV                        | 38.6| 46.8| 34.4| |
| Unrecorded                | 17.8| 8.0| 22.6| |

### Discharge lab value

|                          |    |    |    |     |
|--------------------------|----|----|----|-----|
| Potassium, mEq/L, median, IQR | 5.1 (4.3, 5.3) | 5.1 (4.5, 5.3) | 5.0 (4.2, 5.3) | 0.047 |
| Serum creatine, mg/dL, median, IQR | 2.3 (1.1, 4.0) | 1.3 (1.0, 2.6) | 2.8 (1.2, 4.9) | <0.001 |

### LVEF

|                          |    |    |    |     |
|--------------------------|----|----|----|-----|
| <40%                      | 13.7| 19.1| 11.0| |
| ≥40%, <50%                | 10.4| 13.0| 9.1| |
| ≥50%                      | 35.2| 24.1| 35.8| |
| unmeasured                | 40.7| 33.8| 44.1| |
| Medications at discharge (%) |   |   |   |
|-----------------------------|---|---|---|
| 25.9 | 48.8 | 14.5 | <0.001 |
| 29.3 | 45.1 | 21.5 | <0.001 |
| 36.1 | 69.2 | 19.6 | <0.001 |
| 8.5 | 20.7 | 2.5 | <0.001 |

NYHA indicates New York Heart Association; LVEF, left ventricular ejection fraction; ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.
Figure S1. Spironolactone prescription at discharge among ideal patients with HF by hospital subtype

CABG indicates coronary artery bypass graft.
Figure S2. Spironolactone prescription at discharge among contraindicated patients with HF by hospital subtype

CABG indicates coronary artery bypass graft.