Intravenous Fluids in Acute Decompensated Heart Failure

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Abstract

OBJECTIVES

This study sought to determine the use of intravenous fluids in the early care of patients with acute decompensated heart failure (HF) who are treated with loop diuretics.

BACKGROUND

Intravenous fluids are routinely provided to many hospitalized patients.

METHODS

We conducted a retrospective cohort study of patients admitted with HF to 346 hospitals from 2009 to 2010. We assessed the use of intravenous fluids during the first 2 days of hospitalization. We determined the frequency of adverse in-hospital outcomes. We assessed variation in the use of intravenous fluids across hospitals and patient groups.

RESULTS

Among 131,430 hospitalizations for HF, 13,806 (11%) were in patients treated with intravenous fluids during the first 2 days. The median volume of administered fluid was 1,000 ml (interquartile range: 1,000 to 2,000 ml), and the most commonly used fluids were normal saline (80%) and half-normal saline (12%). Demographic characteristics and comorbidities were similar in hospitalizations in which patients did and did not receive fluids. Patients who were treated with intravenous fluids had higher

rates of subsequent critical care admission (5.7% vs. 3.8%; p < 0.0001), intubation (1.4% vs. 1.0%; p = 0.0012), renal replacement therapy (0.6% vs. 0.3%; p < 0.0001), and hospital death (3.3% vs. 1.8%; p < 0.0001) compared with those who received only diuretics. The proportion of hospitalizations that used fluid treatment varied widely across hospitals (range: 0% to 71%; median: 12.5%).

CONCLUSIONS

Many patients who are hospitalized with HF and receive diuretics also receive intravenous fluids during their early inpatient care, and the proportion varies among hospitals. Such practice is associated with worse outcomes and warrants further investigation. (J Am Coll Cardiol HF 2015;3:127–33) © 2015 by the American College of Cardiology Foundation.

Keywords: diuretics, heart failure, intravenous fluids

Many signs and symptoms of heart failure (HF) are the result of volume overload [1]. Diuretic therapy, which reduces excess volume, is the most common treatment applied to improve symptoms and cardiovascular function [2,3]. For patients treated with diuretics, the administration of intravenous fluids is counterintuitive. Although some studies have investigated the benefits of co-administration of small volumes of hypertonic saline [4,5], the guidelines generally suggest fluid restriction for patients with HF and do not generally recommend intravenous fluid therapy [6–8]. However, intravenous fluids are routinely administered to hospitalized patients [9,10], and little is known about the frequency with which this occurs in patients with HF who are treated with diuretics. If this practice were common, it could indicate conflicting treatment patterns.

We investigated the frequency and pattern of early treatment with intravenous fluids among inpatients with HF who received loop diuretic therapy in a national sample of hospitals. We focused on early treatment to avoid treatments that are in response to changes in the clinical condition of the hospitalized patient, such as use of fluids in response to intensive diuretic therapy. We also examined the association between the early administration of intravenous fluids and in-hospital events, including subsequent critical care admission, subsequent endotracheal intubation, subsequent renal replacement therapy, and in-hospital death. Further, we examined the variability in hospital rates of intravenous fluid administration in patients who concomitantly received loop diuretics.

METHODS

DATA SOURCE AND STUDY SAMPLE

We conducted a retrospective cohort study using a database created by Premier, Inc. (Charlotte, North Carolina) that roughly represents 20% of annual acute care hospitalizations in the United States. In addition to information available in the standard hospital discharge file, the database contains a date-stamped log of all billed items at the patient level, including diagnostic tests, medications, and therapeutic services [11].

We included hospitalizations from 2009 and 2010 for patients age 18 years or older with a principal discharge diagnosis of HF, as defined by International Classification of Diseases-Ninth Revision-Clinical Modification (ICD-9-CM) codes 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, or 428.xx, who were treated with loop diuretic therapy in the first 2 days of hospitalization. Hospitalizations were excluded if the patients were hospitalized for <2 days, had a pediatric attending physician, or were transferred in. We focused on patients who were stable and excluded those who may have received intravenous fluids for another reason such as invasive cardiovascular procedures in the first 2 days; those with a secondary discharge diagnosis of sepsis, bleeding, or anaphylaxis; and those who received vasopressor or inotrope therapies. We excluded patients who had ICD-9-CM codes for stage 5 chronic kidney disease or end-stage renal disease because the use of diuretics and fluids is largely driven by kidney function status in such patients (Online Appendix 1). We also excluded hospitalizations during which patients had a critical care admission in the first 2 days, underwent endotracheal intubation in the

first 2 days, or received renal replacement therapy in the first 2 days because we were interested in studying in-hospital outcomes of new critical care admission, new intubation, and new dialysis after the first 2 days.

INTRAVENOUS FLUID USE, LOOP DIURETIC USE, AND CLASSIFICATION OF TREATMENT INTENSITY

We defined intravenous fluid use as any use ≥500 ml of normal saline, half-normal saline solution, Ringer's/lactated Ringer's, or a combination of these solutions during the first 2 days of hospitalization, using 34 different administrative codes for intravenous fluids. We selected the volume cutoff to ensure that we captured fluid use that was administered for fluid management rather than for administration of other medications such as antibiotics or intravenous antiarrhythmics ([12]). We did not include codes related to administration of dextrose 5% solution because dextrose 5% would minimally enhance the intravascular volume.

We defined loop diuretic use as any use of furosemide, bumetanide, torsemide, or a combination during the first 2 days. In line with published studies, we converted the doses of bumetanide and torsemide to bioequivalent doses of furosemides: 40 mg intravenous furosemide = 80 mg oral furosemide = 20 mg (oral or intravenous) torsemide = 1 mg (oral or intravenous) bumetanide ([13–15]).

OUTCOME MEASURES

Our primary outcome was the proportion of hospitalizations in which patients were treated with intravenous fluids in the first 2 days of hospitalization. We noted the dose of each treatment over the first 2 days.

Secondary outcomes included length of stay, in-hospital death, and receipt of subsequent (after day 2) critical care admission, intubation, and renal replacement therapy by treatment group (i.e., fluid treatment or no fluid treatment). We also determined the risk-standardized utilization rates of intravenous fluids across hospitals.

STATISTICAL ANALYSES

We calculated summary statistics for categorical variables using frequencies and percentages. We used a chi-square test to determine differences between treatment groups for unadjusted outcomes and hierarchical logistic regression to calculate adjusted odds ratios for all outcomes and to calculate hospital-level fluid utilization rates. We calculated odds ratios and 95% confidence intervals (CIs) of the fluid treatment versus no fluid treatment group for each outcome. Each patient could have been hospitalized more than once during the study period, although the majority had a single hospitalization. We used all hospitalizations when calculating odds ratios for renal replacement therapy, admission to an intensive care unit, and late intubation, and 1 randomly selected hospitalization per patient when calculating odds ratios for in-hospital mortality. We adjusted for clinically pre-specified patient characteristics and comorbidities ([Table 1]). A p value of <0.05 was considered statistically significant; however, no adjustment for multiple comparisons was made. Interpretation of the results should take this into consideration.

TABLE 1

Patient Characteristics (N = 131,430)

	Overall (n = 131,430)	Patients Treated With IV Fluids[*] (n = 13,806)	Patients Not Treated With IV Fluids[*] (n = 117,624)
Age, yrs			
18–54	14,127 (11)	1,439 (10)	12,688 (11)
55–64	17,156 (13)	1,805 (13)	15,351 (13)
65–74	25,454 (19)	2,712 (20)	22,742 (19)
75–84	38,189 (29)	3,950 (29)	34,239 (29)
85+	36,504 (28)	3,900 (28)	32,604 (28)
Sex			
Female	69,408 (53)	7,521 (54)	61,887 (53)
Male	62,021 (47)	6,285 (46)	55,736 (47)
Race			
White	83,262 (63)	8,599 (62)	74,663 (63)
Black	24,680 (19)	2,199 (16)	22,481 (19)
Hispanic	5,967 (5)	731 (5)	5,236 (4)
Other	17,521 (13)	2,277 (16)	15,244 (13)
Comorbidities			
Obesity	22,237 (17)	2,258 (16)	19,979 (17)
Diabetes with and without complications	59,041 (45)	6,181 (45)	52,860 (45)

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Values are n (%).

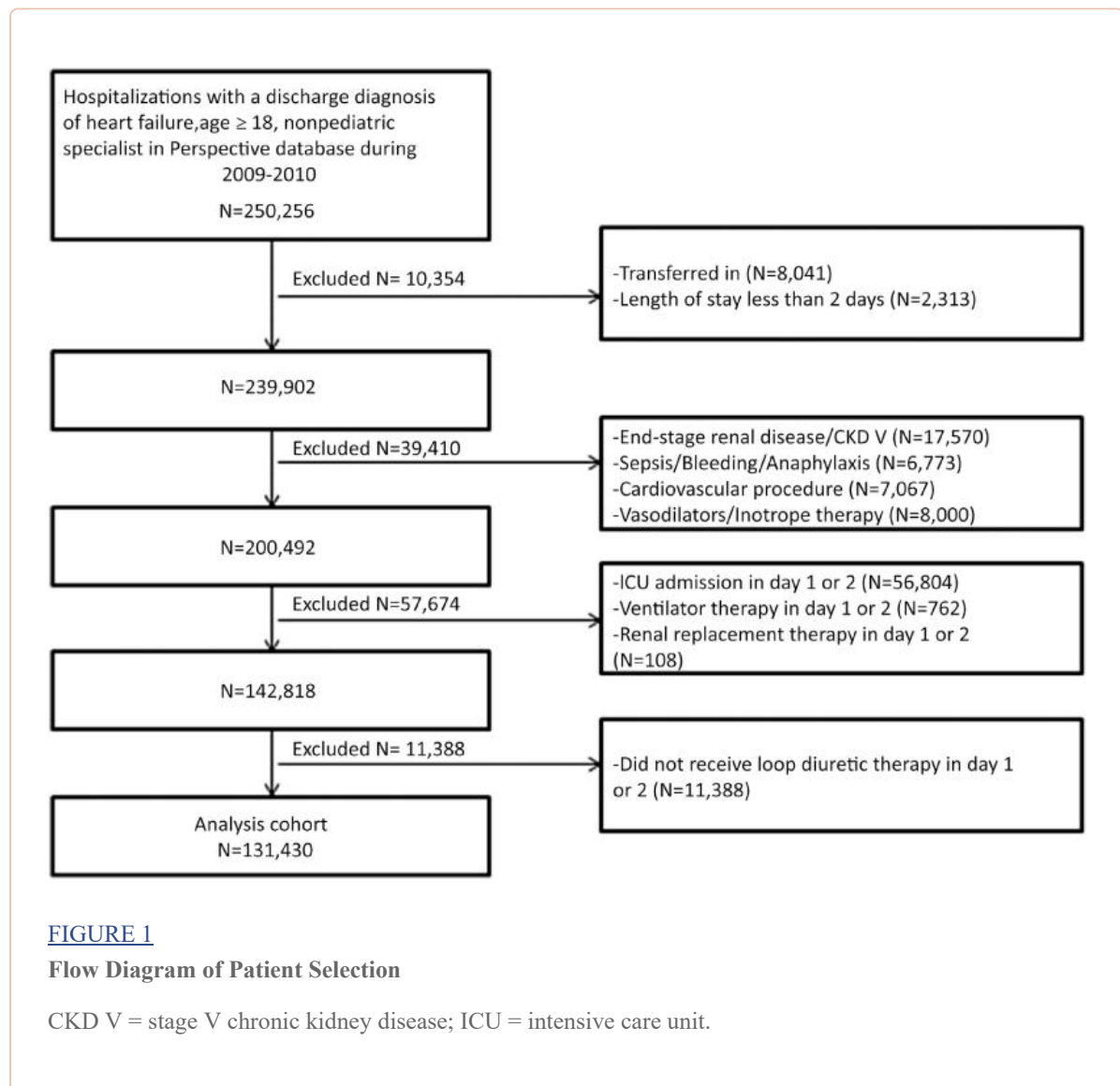[*]All patients were treated with loop diuretics.

IV = intravenous.

K.M.S. and S.L. conducted the analyses with SAS version 9.2 (SAS Institute, Inc., Cary, North Carolina). The Yale University Human Investigation Committee (New Haven, Connecticut) reviewed the study protocol and determined that it was not considered Human Subjects Research as defined by the Office of Human Research Protections.

RESULTS

COHORT SELECTION AND BASIC CHARACTERISTICS

We identified 250,256 hospitalizations with HF in which patients were 18 years or older and had a nonpediatric attending physician in the 2009 to 2010 database. After applying the exclusions, there were 131,430 hospitalizations in the final cohort (Figure 1). The majority of patients were older than 75 years (57%), female (53%), and white (63%) (Table 1). The most common comorbidity was hypertension (70%), followed by diabetes (45%). The group that received intravenous fluids had demographic characteristics that were similar to those of the group that did not receive intravenous fluids (see Table 1).

FIGURE 1

Flow Diagram of Patient Selection

CKD V = stage V chronic kidney disease; ICU = intensive care unit.

TREATMENT WITH INTRAVENOUS FLUIDS AND LOOP DIURETICS

Patients received intravenous fluid therapy in 11% of hospitalizations, of which 80% involved normal saline solution as the only fluid treatment and 91% involved furosemide as the only loop diuretic (Table 2). For hospitalizations in which patients received intravenous fluids, the median total intravenous fluid volume was 1,000 ml (interquartile range [IQR]: 1,000 to 2,000 ml) during the first 2 days, and the median total diuretic dose in intravenous furosemide-equivalent doses was 120 mg (IQR:

80 to 200 mg) over the first 2 days. The median total loop diuretic dose in intravenous furosemide-equivalent doses for those who did not receive intravenous fluids was 140 mg (IQR: 80 to 210 mg) during the first 2 days.

TABLE 2

Loop Diuretic and Fluid Utilization Among Hospitalizations in Which Patients Received Intravenous Fluids (N = 13,806)

Type of Therapy	Utilization
Diuretic therapy	
Furosemide	12,534 (91)
Bumetanide	488 (3)
Torsemide	85 (1)
Mixed[*]	699 (5)
Fluid therapy	
Normal saline solution	11,097 (80)
Half-normal saline solution	1,591 (12)
Ringer's/lactated Ringer's	226 (2)
Mixed[†]	892 (6)

Values are n (%).

[*]Defined as any combination of loop diuretics.
[†]Defined as any combination of intravenous fluids.

OUTCOMES

Median hospital length of stay was 4 days (IQR: 3 to 7 days) among hospitalizations in which patients received intravenous fluids and 4 days (IQR: 2 to 6 days) among hospitalizations in which patients did not receive intravenous fluids. Hospitalizations in which patients received intravenous fluids were associated with higher rates of subsequent critical care admission (5.7% vs. 3.8%; p < 0.0001), late intubation (1.4% vs. 1.0%; p = 0.0012), renal replacement therapy (0.6% vs. 0.3%; p < 0.0001), and in-hospital mortality (3.3% vs. 1.8%; p < 0.0001) compared with hospitalizations in which the patient did not receive intravenous fluids.

After adjusting for demographics and comorbidities, hospitalized patients who received intravenous fluids were, after day 2, 1.57 (95% CI: 1.45 to 1.71) times more likely to be admitted to critical care, 1.46 (95% CI: 1.25 to 1.71) times more likely to undergo intubation, 2.04 (95% CI: 1.62 to 2.55) times more likely to receive renal replacement therapy, and 2.02 (95% CI: 1.82 to 2.24) times more likely to experience in-hospital death compared with hospitalized patients who did not receive intravenous fluids (Table 3).

TABLE 3

Risk-Adjusted Hospitalization Outcomes by Therapy

|	Critical Care Admission[*]	Late Intubation	Renal Replacement Therapy	In-Hospital Death
No treatment with intravenous fluids[†]	–	–	–	–
Treatment with intravenous fluids[†]	1.57 (1.45–1.71)	1.46 (1.25–1.71)	2.04 (1.62–2.55)	2.02 (1.82–2.24)

Values are odds ratio (95% confidence interval).

[*]Includes admission to step-down units.
[†]All patients were treated with loop diuretics.

TREATMENT WITH INTRAVENOUS FLUIDS ACROSS HOSPITALS

Across hospitals with at least 25 HF hospitalizations during the study period, the risk-standardized fluid utilization rate ranged from 0% to 71.1%, with a median of 12.5% (Figure 2).
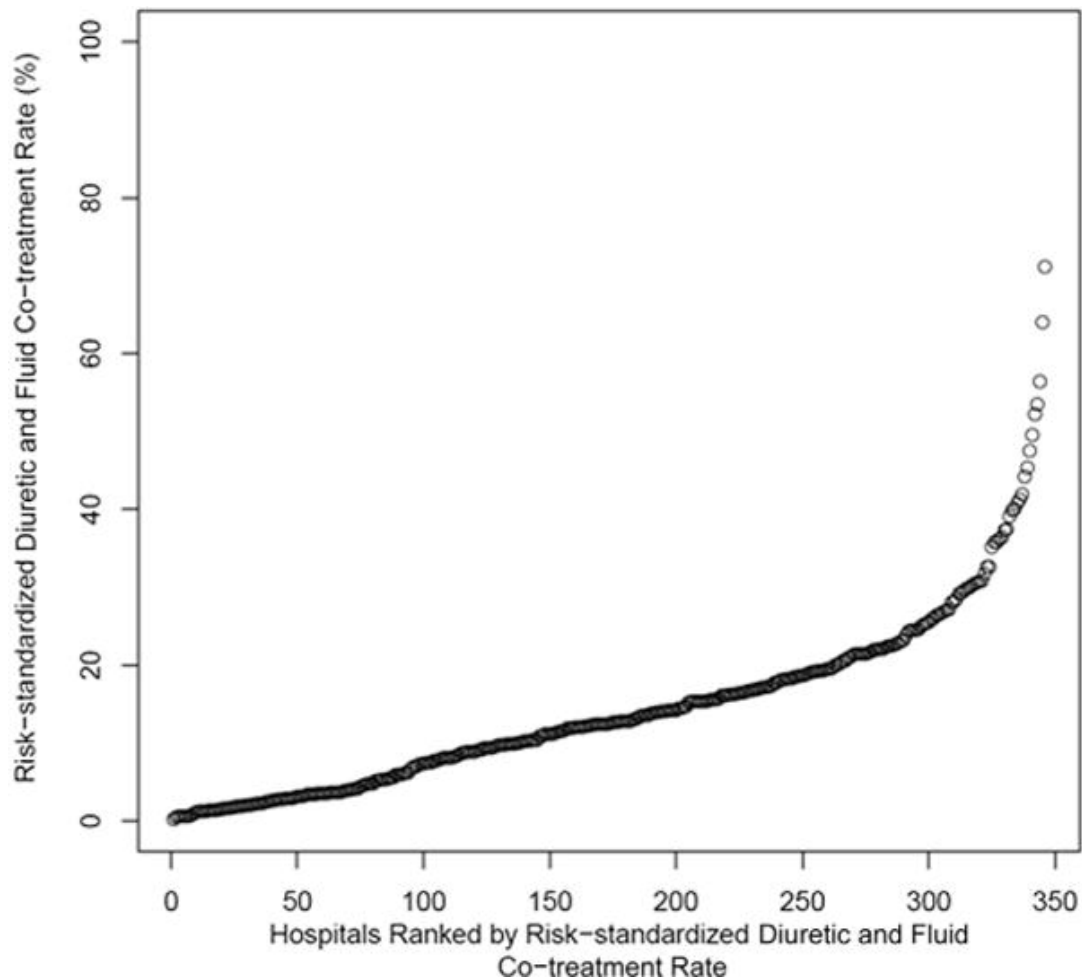
FIGURE 2

Intravenous Fluid Administration Rate by Hospital (N = 346)

Each **circle** represents a hospital.

DISCUSSION

Among hospitalizations for acute decompensated HF in which patients were treated with loop diuretics in the first 2 days, we found that 11% were also given volumes of intravenous fluids (median: 1,000 ml) that were neither negligible nor used primarily for administration of other therapies. The remarkable variation among hospitals suggests that factors beyond differences in patient populations influence co-administration of fluids and diuretics.

Our study is the first to investigate the use of intravenous fluids among patients hospitalized with decompensated HF. Because fluid overload is a major contributor to acute decompensation in patients with HF (8), the administration of intravenous fluids in addition to loop diuretic therapy is an unanticipated observation. There are several possible explanations for the considerable rate of intravenous fluid administration in acutely decompensated inpatients with HF. First, some patients may have received fluids because of hemodynamic instability. We excluded patients most likely to have hemodynamic instability (i.e., those with discharge diagnoses of bleeding, sepsis, or anaphylaxis), as well as those who underwent invasive cardiovascular procedures and who received vasopressor or inotropic treatment in the first 2 days. Nevertheless, it is still likely that some unstable patients remained in our study cohort. Second, fluids could have been administered to some patients with acute decompensated right ventricular failure. However, this is not likely to reflect a large proportion of the study patients who received treatment with intravenous fluids. Usually, patients with acute right

ventricular failure need inotrope or vasopressor therapy and, accordingly, we excluded those who received inotropes or vasopressors during the first 2 days (16). Third, fluids may have been administered to counter the detrimental effects of excessive loop diuretic therapy, but we did not observe a difference in the loop diuretic dose between the 2 groups. Further, our examination of use of intravenous fluids during the first 2 days of hospitalization minimized the possibility of including fluid therapy that was administered in response to excessive diuresis. Another possibility is the inadvertent administration of intravenous fluids.

Finally, it is possible that the concomitant use of diuretics and fluids was a purposeful treatment strategy. Although several small studies have shown hemodynamic and clinical improvement in patients receiving co-treatment with loop diuretics and small volumes of intravenous hypertonic saline (4,5,17,18), the amounts of fluid were very small (100 to 150 ml twice daily), and the small volume of hypertonic fluid introduced a notable amount of salt for the treated patients, unlike the fluids that we studied. Because of using administrative data, we are, however, unable to specify the reasons for use of intravenous fluids in each of the patients in our cohort.

We observed higher rates of late critical care admission, late intubation, late renal replacement therapy, and in-hospital death for patients who received intravenous fluids compared with those who did not. One possibility, consistent with expert opinion, is that fluid overload may directly worsen the clinical outcomes of patients with HF (6–8,19), who are commonly volume overloaded. However, it is also possible that the administration of fluids is a marker of greater clinical severity rather than a cause of worse outcomes. Although we had used rigorous inclusion and exclusion criteria to minimize the possibility of having unstable patients in our cohort, our findings should not be considered causal at this stage.

STUDY LIMITATIONS

Our results need to be interpreted in the context of the study limitations. Our study identified that intravenous fluids are administered in 11% of hospitalizations for patients with acute decompensated HF who are treated with loop diuretics. We believe that the rates of intravenous fluid use would have been even higher had we not excluded hospitalizations in patients who were more likely to be unstable (e.g. those receiving inotropes). Although we were unable to distinguish between the types of HF (i.e., HF with preserved versus reduced ejection fraction), previous studies have shown the high specificity of the codes we used for principal diagnosis of HF among hospitalized patients (20–22). Another limitation of our study was lack of access to kidney function biomarkers, left ventricular function indices, and hemodynamic parameters such as heart rate or blood pressure. Availability of these indices could have been helpful for further mechanistic evaluations and prognostication. Despite not having access to such variables, however, we minimized the chance of including hemodynamically unstable patients by excluding those who received vasopressor or inotrope therapy, those who underwent invasive cardiovascular procedures, and those with discharge diagnoses of sepsis, bleeding, or anaphylaxis. Even if we overestimated the problem because of lack of clinical information that could explain the use of intravenous fluids in some patients, it is important in its magnitude. It should be mentioned that our final cohort, built using these inclusions and exclusions, had similar characteristics compared with patients in existing HF registries, such as the ADHERE (Acute Decompensated HEart failure REgistry). (13). Another limitation of our study is the use of billing to determine fluid administration rather than direct observation. It is possible that in some cases, the fluid was dispensed but not administered or partially used. Even in the unlikely event that this attribution error commonly occurred, the rates of fluid administration to patients with HF are sufficiently high to indicate a need for further examination.

Finally, as stated earlier, the associations that we observed should not be considered causal. Although it is possible that inadvertent use of fluids may lead to worse outcomes, there are other potential explanations that, despite our exclusion and inclusion criteria, cannot be eliminated. Until we have further data from future prospective investigations, decisions about the use of intravenous fluids in patients with decompensated HF remain a challenge and should be made on a case-by-case basis with respect to factors such as HF status and renal function. Whereas practitioners may deliberately choose to administer intravenous fluids for patients with HF who may need such therapy, it appears prudent for

hospitals to implement strategies that would help minimize the possibility of inadvertent intravenous fluid therapy. These would include review of standard emergency department order sets that could routinely call for intravenous fluids, as well as use of automated reminders that could help minimize unnecessary administration of fluids to patients with decompensated HF.

CONCLUSIONS

We found that the administration of fluids to patients admitted with HF is not uncommon and varies substantially across hospitals, with potential adverse consequences. This practice may occur inadvertently for many patients, warrants further investigation, and may be an opportunity for improvement.

Supplementary Material

Bikdeli_supplemental file

[Click here to view.](33K, docx)

Acknowledgments

ABBREVIATIONS AND ACRONYMS

HF   heart failure

ICD-9-CM   International Classification of Diseases-Ninth Revision-Clinical Modification

Footnotes

During the time the work was conducted, Drs. Bikdeli and Mody were post-doctoral associates, Dr. Dharmarajan was a post-doctoral fellow, and Dr. Partovian was an instructor in the Section of Cardiovascular Medicine, Department of Internal Medicine, Yale University School of Medicine in New Haven, Connecticut.

All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

APPENDIX For a list of cardiovascular procedures and a list of International Classification of Diseases-Ninth Revision-Clinical Modification codes indicating stage V or end-stage renal disease, please see the online version of this paper.

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