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MINI-FOCUS ISSUE: PREVENTING HEART FAILURE ADMISSIONS

Intravenous Diuretic Therapy for the Management of Heart Failure and Volume Overload in a Multidisciplinary Outpatient Unit

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ABSTRACT

OBJECTIVES This study sought to evaluate the effectiveness of intravenous (IV) diuretic treatment for volume management in heart failure (HF).

BACKGROUND Limited data exist regarding IV diuretics for the outpatient treatment of volume overload in HF patients.

METHODS We analyzed 60 consecutive patients with chronic HF and clinical evidence of worsening congestion who received a bolus and 3-h IV infusion of furosemide at an outpatient HF clinic. Diuretic dosing was derived from the maintenance oral loop diuretic dose with a standardized conversion algorithm. Outcomes included urine output during the visit, weight loss at 24 h, and hospitalization and mortality at 30 days. Safety outcomes included hypokalemia and worsening of renal function. Outcomes were analyzed across subgroups defined by maintenance diuretic dose and ejection fraction (EF).

RESULTS The median age of the cohort was 70 years (interquartile range [IQR]: 58 to 80 years), and the median daily loop diuretic dose was 240 mg (IQR: 80 to 800 mg) oral furosemide or equivalent. Twenty-six patients (43.3%) were women, and 36 (60%) had an EF ≤45%. For the entire cohort, the median urine output and 24-h weight loss were 1.1 l (IQR: 0.6 to 1.4 l) and 1.1 kg (IQR: 0.2 to 1.9 kg), respectively. Outcomes were similar across patients with varying maintenance diuretic doses (<40 mg, 40 to 160 mg, 160 to 300 mg, or >300 mg of furosemide or equivalent) and in patients with reduced or preserved EF. Transient worsening of renal function and hypokalemia occurred in 10 patients (8.9%) and 4 patients (3.5%). Although hospitalization was reported as imminent for 28 patients (52.8%), the observed rate of all-cause hospitalization was 31.7% at 30 days with no deaths.

CONCLUSIONS Short courses of IV diuretics for volume management in patients with HF were safe and associated with significant urine output and weight loss across a wide range of maintenance diuretic doses and EF. This strategy may provide an alternative to hospitalization for the management of selected HF patients. (J Am Coll Cardiol HF 2016;4:1–8)

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ABBREVIATIONS AND ACRONYMS

HF = heart failure

HFpEF = heart failure with preserved ejection fraction

HFrEF = heart failure with reduced ejection fraction

IQR = interquartile range

IV = intravenous

Since heart failure (HF)-related hospitalizations typically result from worsening congestion, loop diuretics are administered as the mainstay of therapy in 90% of HF hospitalizations (1,2). Fiscal incentives to reduce the burden of hospital admissions for HF management have fueled interest in ambulatory strategies for the management of HF decompensation, including clinic-based administration of intravenous (IV) diuretics (3–7).

Limited data are available regarding the use of IV diuretics for the ambulatory treatment of decompensated HF (3–8). Although several studies provide clinicians with guidance on diuretic dosing strategies for hospitalized patients, no such guidance exists for use in ambulatory patients (9–12). It also remains unclear whether a strategy of ambulatory IV diuretic administration is a reasonable alternative to hospital admission for selected patients with worsening HF. In this paper, we report on the safety and efficacy of IV diuretic administration according to a standardized dosing guideline used in our ambulatory HF treatment unit.

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METHODS

SETTING. The Ambulatory Cardiac Triage, Intervention, and Education (ACTIVE) Unit at Brigham and Women's Hospital is an ambulatory treatment clinic that provides advanced care to patients with early HF decompensation. The Brigham and Women's Heart and Vascular Center provided funding for this initiative. Eligible patients include hemodynamically stable (systolic blood pressure >90 mm Hg) ambulatory patients with chronic HF (regardless of left ventricular ejection fraction [EF]) and clinical signs and symptoms of worsening congestion. Patients with advanced or end-stage chronic kidney disease, concern for an acute cardiovascular or medical condition precipitating HF (e.g., new-onset arrhythmia, acute coronary syndrome, pulmonary embolism), severe symptoms, massive volume overload (e.g., >10 to 15 lb of estimated fluid weight) or anasarca, need for emergent medical treatment, or perceived high risk of clinical instability with outpatient treatment are instead referred to the emergency department or inpatient ward for further evaluation.

A multidisciplinary team of physicians, pharmacists, and nurses provides a comprehensive package of services to patients with advanced HF. The dedicated clinic space includes 2 infusion chairs with cardiac telemetry, local medication storage, infusion equipment, and an en suite bathroom. The unit can accommodate up to 4 patients per day (2 in the morning session and 2 in the afternoon session) for a 3-h IV diuretic infusion. Patients are typically scheduled for same-day or next-day treatment depending on the time of presentation to the ambulatory cardiovascular clinics and are rebooked for repeat visits as needed. Direct patient care is provided by a dedicated nurse, with supervision from a specialized nurse practitioner. At each clinic visit, nurses place an IV line, obtain a detailed medical history, provide HF education, administer medications, and monitor cardiac telemetry. A clinical pharmacist performs a detailed medication reconciliation, evaluates medication adherence, provides medication education, and optimizes medications for comorbid conditions with careful attention to drug interactions. Specialty consultation with nutrition, diabetes, and palliative care specialists is arranged on an as-needed basis.

STUDY PATIENTS. All patients who received treatment with IV furosemide in the Brigham and Women's Hospital ACTIVE Unit between September 1, 2013 and February 15, 2014 were included in this analysis. Electronic medical records were reviewed for patient demographic characteristics and outcomes.

INTERVENTIONS. IV furosemide doses were determined according to a standardized protocol based on the patient's home diuretic dose (**Figure 1**). Patients were assigned to 1 of 4 protocol groups based on their total daily dose of home oral diuretic (maintenance dose). All doses were expressed in milligrams of oral furosemide, and torsemide or bumetanide doses were converted to an equivalent furosemide dose using standard conversion guidelines (oral furosemide 80 mg = IV furosemide 40 mg = IV torsemide 20 mg = IV bumetanide 1 mg).

Patients in the low-dose group (maintenance dose ≤40 mg) received an IV bolus of furosemide 40 mg followed by a 60-mg infusion delivered over 3 h. Standard-dose group patients (maintenance dose, 41 to 160 mg) received a furosemide IV bolus dose that was equivalent numerically to the oral maintenance dose (in furosemide equivalents) with a 3-h continuous infusion at a rate of 20 mg/h. High-dose group patients (maintenance dose, 161 to 300 mg) received an IV bolus of furosemide 200 mg followed by a 3-h continuous infusion at a rate of 20 mg/h. If high-dose patients had inadequate urine output after 90 min of the continuous infusion, they were eligible to receive a second IV bolus of furosemide 200 mg. Patients with a maintenance dose >300 mg furosemide equivalent were categorized into the mega-dose group and were eligible for optional premedication with a

thiazide diuretic (hydrochlorothiazide, metolazone, or chlorothiazide) in addition to the same IV furosemide regimen as patients in the high-dose group. All patients had labs drawn before the initiation of diuretic treatment and received oral electrolyte repletion during the visit as required according to a standardized protocol (Online Appendix). This protocol was developed by the ACTIVE steering group based on dosages reported in previous studies, our hospital drug administration policies, and group consensus (9).

OUTCOMES. The efficacy outcomes included urine output and weight loss. Urine output was reported as the total volume of urine collected during the clinic visit. Weight loss was measured both at the end of the clinic visit and at 24 h. Clinic weight loss was defined as the difference between the patient's weight at the beginning of and at the end of the clinic visit. Home weight loss was defined as the difference between the patient's weight the morning of and the day after the clinic visit.

Safety outcomes were evaluated within 7 days of each clinic visit. Treatment-related hypokalemia was defined as mild (serum potassium ≤3.5 mEq/l but >3.0 mEq/l at the first lab draw after the clinic visit with a decrease of ≥0.5 mEq from baseline) or severe (serum potassium ≤3.0 mEq/l at the first lab draw after clinic visit with a decrease of ≥0.5 mEq). Worsening of renal function was defined based on the difference between serum creatinine on the day of the clinic visit and the first lab draw after the clinic visit and categorized as either severe (doubling of serum creatinine) or mild (increase in serum creatinine ≥0.3 mg/dl but not a doubling). Ototoxicity was defined as a self-reported acute change in hearing that prompted a new encounter with a health care provider and was not attributable to a cause other than diuretic therapy.

At the time of initial referral, clinicians were asked to indicate whether they would have referred the patient for emergency department evaluation or hospital admission without the option for intravenous ambulatory treatment. The rate of affirmative responses to this query served as the "expected" rate of hospitalization for this cohort. Actual rates of hospitalizations (HF related and all cause) and mortality (all cause) were evaluated at 30 and 60 days from the last visit of each unique treatment episode. Rates of hospitalization and mortality were separately examined in the subgroup of patients with urine output >50% of the median and those with urine output ≤50% of the median.

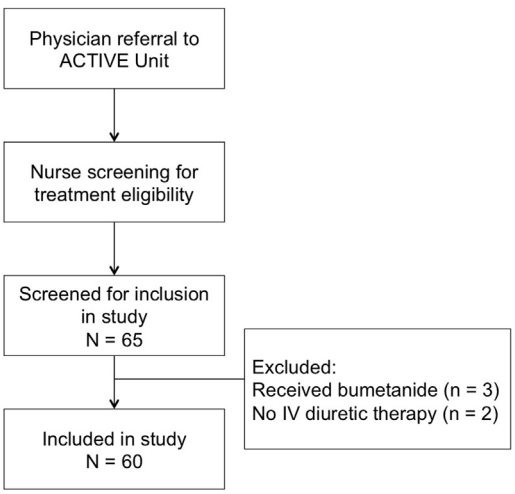
MONITORING. Heart rate, blood pressure, and respiratory rate were measured at 30-min intervals throughout the clinic visit. Patients were monitored on cardiac telemetry during the entire clinic visit. All urine was collected during the visit to accurately quantify urine volume in response to diuretic administration. Laboratories to assess electrolytes and renal function were drawn before the infusion and again within 7 days of the clinic visit for assessment of safety outcomes. All patients received telephone or clinic-based follow-up 30 days after their initial clinic visit to quantitate symptom burden and assess rates of hospitalizations and other adverse events.

FIGURE 1 Standardized IV Diuretic Administration Protocol

Category	Maintenance diuretic dose (mg)*	IV furosemide dose Bolus (mg)	Infusion (mg/hr)	Optional†
Low dose	≤ 40	20	20	--
Standard dose	41-160	Numeric equivalent of maintenance diuretic dose	20	--
High dose	161-300	200	20	200 mg
Mega dose	≥ 301	200	20	200 mg Thiazide diuretic‡

Doses of IV furosemide were determined from the patient's home oral diuretic dose. Graded increases in IV doses corresponded to increases in the patient's maintenance diuretic dose. Infusions were administered over 3 h. *Total daily dose expressed in the equivalent of milligrams of oral furosemide. †If inadequate urine output after 90 min of infusion. ‡Metolazone, 1.25 to 10 mg; hydrochlorothiazide, 12.5 to 50 mg; chlorothiazide, 1,000 mg orally or 500 mg IV. IV = intravenous.

FIGURE 2 Screening and Enrollment



Consecutive patients who were treated with intravenous furosemide at an ambulatory heart failure unit for worsening congestion were included in this study. Patients were referred at the discretion of their cardiologist and screened for eligibility by a nurse prior to treatment. ACTIVE = Ambulatory Cardiac Triage, Intervention, and Education; IV = intravenous.

TABLE 1 Patient Demographics

Demographic Characteristics	All Patients (N = 60)	HFrEF (n = 36)	HFpEF (n = 24)
Age, yrs	70 (60-80)	75 (56-80)	70 (63-79)
Female	26 (43.3)	9 (25)	17 (70.8)
Ethnicity			
African American	9 (15)	5 (13.9)	4 (16.7)
Hispanic	6 (10)	2 (5.6)	4 (16.7)
Caucasian	45 (75)	29 (80.6)	16 (66.7)
Median ejection fraction, %	–	25 (20-31)	55 (55-60)
NYHA functional class			
I	0	0	0
II	7 (11.7)	4 (11.1)	3 (12.5)
III	35 (58.3)	21 (58.3)	14 (58.3)
IV	12 (20)	9 (25)	3 (12.5)
Unknown	6 (10)	2 (5.5)	4 (16.7)
Comorbidities			
Atrial fibrillation	29 (48.3)	18 (50)	11 (45.8)
Chronic kidney disease	28 (46.7)	18 (50)	10 (41.7)
Diabetes mellitus	31 (51.7)	17 (47.2)	14 (58.3)
Hypertension	46 (76.7)	26 (72.2)	20 (83.3)
Pulmonary hypertension	6 (10)	1 (2.8)	5 (20.8)
Chronic obstructive pulmonary disease	12 (20)	3 (8.3)	9 (37.5)
Coronary artery disease	31 (51.7)	20 (55.5)	11 (45.8)
Loop diuretic			
Torsemide	38 (63.3)	24 (66.7)	14 (58.3)
Furosemide	21 (35.0)	12 (33.3)	9 (37.5)
No loop diuretic	1 (1.7)	0	1 (4.2)
Loop diuretic dose, mg/dl*	240 (80-800)	280 (95-800)	240 (80-560)
Therapies			
Thiazide diuretic	13 (21.7)	8 (22.2)	5 (20.1)
ACE inhibitor/ARB	27 (45)	17 (47.2)	10 (41.7)
Aldosterone antagonist	22 (36.7)	15 (41.7)	7 (29.2)
Beta-blocker	48 (80)	33 (91.7)	15 (62.5)
Digoxin	11 (18.3)	10 (27.8)	1 (4.2)
Isosorbide	8 (13.3)	6 (16.7)	2 (8.3)
Hydralazine	3 (5)	3 (8.3)	0
ICD	31 (51.7)	28 (77.8)	3 (12.5)
CRT	16 (26.7)	17 (47.2)	0
Laboratory values			
Serum sodium, mmol/l	138 (135-140)	138 (134-140)	139 (137-140)
Blood urea nitrogen, mg/dl	33 (23-44)	34 (27-46)	28 (22-39)
Serum creatinine, mg/dl	1.44 (1.43-3.95)	1.59 (1.23-2.02)	1.29 (1.04-1.63)
NT-proBNP, pg/ml	3,533 (1,617-6,297)	4,694 (2,714-6,699)	1,545 (562-3,335)
Systolic blood pressure, mm Hg	124 (112-140)	117 (108-134)	132 (122-144)
Diastolic blood pressure, mm Hg	68 (60-77)	68 (60-75)	69 (62-78)

Values are median (interquartile range) or n (%). *Expressed as milligrams of furosemide or equivalent (oral furosemide 80 mg = intravenous furosemide 40 mg = torsemide 20 mg = bumetanide 1 mg).

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CRT = cardiac resynchronization therapy; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; ICD = implantable cardioverter-defibrillator; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association.

STATISTICAL ANALYSIS. Baseline characteristics were presented in tabular form for the population as a whole, and in subgroups defined by an EF >45% (HF with preserved EF [HFpEF]) or ≤45% (HF with reduced EF [HFrEF]). Efficacy and safety outcomes at 24 h and 30 days were summarized using standard descriptive statistics. Outcomes were compared across maintenance diuretic dose groups with the Kruskal-Wallis test. The Mann-Whitney *U* test was used to compare outcomes across EF (HFrEF vs. HFpEF). The relative risk for hospitalization was calculated by comparing observed rates of 30-day hospitalization with the clinician-predicted rates. A 2-sided p value ≤0.05 was considered to indicate statistical significance.

RESULTS

PATIENT CHARACTERISTICS. Sixty patients who underwent 112 discrete treatment visits were included in the final analysis (Figure 2). Demographic characteristics and visit metrics are summarized in Tables 1 and 2. The median age of all patients was 70 years (interquartile range [IQR]: 60 to 80 years). Patients were predominantly male (56.7%) and Caucasian (75%). The proportion of patients with HFpEF was 40%. Before decompensation, 58.3% of patients reported New York Heart Association functional class III symptoms and 20% of patients reported functional class IV symptoms. Comorbid conditions were common among both HFrEF and HFpEF patients. The median maintenance diuretic dose was 240 mg oral furosemide (IQR: 80 to 800 mg oral furosemide). Torsemide was the maintenance diuretic for 38 patients (63.3%). Thirteen patients (21.7%) were taking metolazone in addition to loop diuretic therapy. Most patients (80%) received treatment over 1 or 2 visits.

OUTCOMES. The outcomes of IV diuretic treatment by clinic visit are described in Table 3, and by protocol group in Table 4. The median urine output was 1,045 ml (IQR: 619 to 1,400 ml). The median clinic weight loss was 1 kg (IQR: 0.6 to 1.3 kg). The median home weight loss was 1.1 kg (IQR: 0.2 to 1.9 kg). There were no differences between patients with HFrEF and HFpEF (Figure 3, Table 3) with respect to urine output ($p = 0.20$), clinic weight loss ($p = 0.24$), or home weight loss ($p = 0.53$). Both the standard-dose and the high-dose groups had more urine output during the 3-h clinic visit than the mega-dose group (1,402 ml [IQR: 1,003 to 1,795 ml] vs. 1,150 ml [IQR: 1,040 to 1,398 ml] vs. 950 ml [IQR: 500 to 1,180 ml], respectively; $p < 0.05$ for both comparisons with the standard-dose group). Clinic weight loss was greater in the standard-dose group compared with the mega-dose group (1.3 kg [IQR: 0.9 to 1.8 kg] vs. 0.9 kg [IQR: 0.4 to 1.2 kg]; $p < 0.05$). There were no statistically significant differences across diuretic dosing subgroups with respect to home weight loss ($p = 0.37$).

Two patients were directly admitted to the hospital after their first ambulatory treatment attempt due to

failure to respond to the diuretic infusion. At 30-day follow-up, 19 total hospitalizations (31.7%) were recorded for the cohort, including 11 (18.3%) for worsening HF, and no deaths (**Figure 4**). At 60-day follow-up, rates of all-cause hospitalization and HF hospitalization were 38.3% and 21.7% with 1 recorded death. For comparison, hospitalization was reported by the referring clinician to be imminent or expected within 30 days of referral for 52.8% of patients (relative risk for all-cause hospitalization for observed vs. predicted: 0.60; 95% confidence interval: 0.38 to 0.94; p = 0.03). There were 3 HF hospitalizations (9.4%) at 30 days and 5 HF hospitalizations (9.4%) at 60 days in patients with urine output greater than the median. Among patients with urine output less than the median, 6 patients (18.2%) at 30 days and 8 patients (24.2%) at 60 days were hospitalized for HF.

The median time to laboratory follow-up was 3 days (IQR: 1 to 4 days). Severe worsening of renal function did not occur after any clinic visits. Mild worsening of renal function occurred after 10 visits (8.9%), including 6 in patients with a history of renal impairment. Serum creatinine returned to baseline for each patient within a median of 4 days (IQR: 3 to 6 days) after initial laboratory follow-up. Mild and severe hypokalemia occurred after 3 (2.7%) and 1 (0.9%) clinic visits, respectively. No clinically significant arrhythmias were noted on telemetry during any of the treatment visits. No episodes of ototoxicity or other serious adverse effects were recorded.

TABLE 2 Visit Metrics

Parameter	All Patients (N = 60)	HFrEF (n = 36)	HFpEF (n = 24)
No. of visits			
1	33 (55)	22 (61.1)	11 (45.8)
2	15 (25)	9 (25)	6 (25)
≥3	12 (20)	5 (13.9)	7 (29.2)
Duration between first and second visits, days	6 (4–13)	6 (4–14)	6 (5–13)
Duration between second and third visits, days	7 (4–27)	7 (4–44)	5 (3–9)
Diuretic therapy			
Total dose, mg*	260 (140–260)	250 (140–260)	240 (130–260)
Low-dose group	11 (18.3)	5 (13.9)	6 (25)
Standard-dose group	13 (21.7)	7 (19.4)	6 (25)
High-dose group	7 (11.7)	6 (16.7)	1 (4.2)
Mega-dose group	29 (48.3)	18 (50)	11 (45.8)
Time to laboratory follow-up, days	3 (1–4)	3 (1–3)	3 (2–4)

Values are n (%) or median (interquartile range). *Milligrams of intravenous furosemide per visit.
Abbreviations as in Table 1.

DISCUSSION

These results demonstrate that a standardized algorithm for IV loop diuretic dosing may be used to achieve decongestion among patients with advanced HF across a wide range of maintenance diuretic doses and independent of EF. Despite the administration of high diuretic doses, hypokalemia and worsening renal function were typically mild and transient (3,4,6–8). While hospitalization was thought to be imminent in more than one-half of patients referred for treatment, observed rates of 30- and 60-day hospitalization were considerably lower after ambulatory IV therapy, with the minority of admissions related to the management of worsening HF. We conclude that ambulatory administration of IV diuretic treatment may be a safe and effective alternative to hospitalization for selected hemodynamically stable patients with worsening HF.

Our study adds to the growing body of evidence supporting the efficacy of ambulatory diuretic treatment for HF. Many patients hospitalized with HF receive little treatment other than IV diuretics and require only episodic surveillance by bedside examination and laboratory testing (13). Few patients require invasive testing or complex hemodynamic monitoring, net weight loss during hospitalization is frequently modest, and patient symptoms are frequently relieved within 24 h of hospital admission (14,15). In the context of these observations and increasing fiscal pressures to reduce treatment costs, there is increasing interest in ambulatory alternatives to hospitalization for the management of patients with worsening HF symptoms (16).

Although others have reported on the use of IV diuretics in the clinic setting (4,6–8), our experience is unique in several respects. First, many of our patients had advanced HF, as indicated by the proportion of patients with New York Heart Association functional class III to IV symptoms at baseline, high burden of comorbidities, and high maintenance loop diuretic doses. A greater proportion of patients treated with torsemide than in other cohorts (17) reflects our institutional bias to substitute torsemide for furosemide in sicker patients with refractory congestion or predominant right HF for whom drug absorption or diuretic resistance is a concern (18). Low rates of angiotensin-converting enzyme inhibitor and angiotensin receptor blocker use by the HFrEF patients (19) in our cohort

TABLE 3 Efficacy Outcomes in All Patients and According to Ejection Fraction

Outcome	All Visits (N = 112)		HFrEF (n = 57)		HFpEF (n = 55)		p Value*
Urine output, ml	1,045	619–1,400	1,000	570–1,395	1,120	785–1,400	0.20
Clinic weight loss, kg	1	0.6–1.3	1.1	0.7–1.5	0.9	0.4–1.3	0.24
Home weight loss, kg	1.1	0.2–1.9	1.1	0.5–1.9	1	0.1–1.8	0.53

Values are median (interquartile range). *p value for comparison of HFrEF with HFpEF.
Abbreviations as in Table 1.

TABLE 4 Efficacy Outcomes According to Protocol Group

Outcome	Low-Dose (n = 13)		Standard-Dose (n = 22)		High-Dose (n = 9)		Mega-Dose (n = 51)		p Value*
Urine output, ml	1,125	825–1,600	1,402	1,003–1,795	1,150	1,040–1,398	95	500–1,180	<0.01†
Clinic weight loss, kg	0.9	0.8–2.5	1.3	0.9–1.8	1.1	0.9–1.3	0.9	0.4–1.2	0.01‡
Home weight loss, kg	1.1	0.7–1.8	1.4	0.6–2.4	1.3	0.4–1.7	0.9	0–1.8	0.37

Values are median (interquartile range). *p value for comparison across protocol groups. †p < 0.05 for comparisons between mega- and standard-dose groups and mega- and high-dose groups. ‡p < 0.05 for comparison between mega- and standard-dose groups.

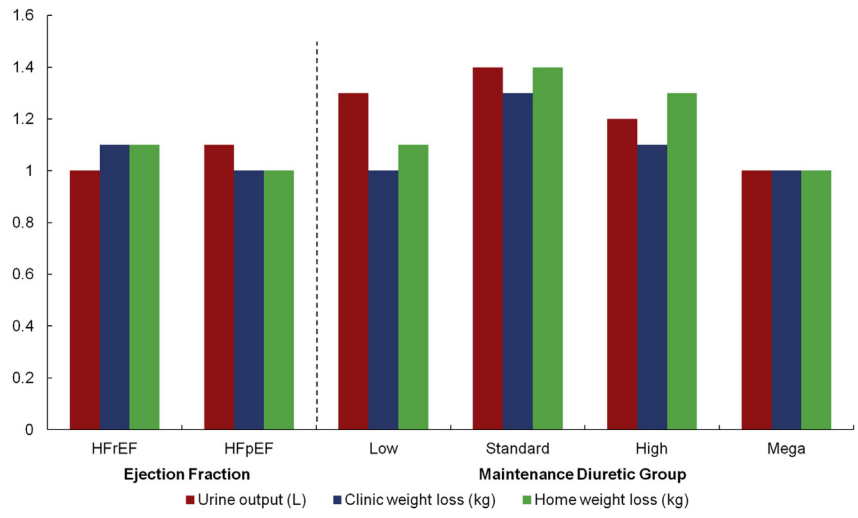
IQR = interquartile range.

were predominantly related to previous intolerance, which is known to be an additional marker of more severe disease (20). Notably, these rates are comparable to those reported in the Acute Decompensated Heart Failure National Registry Longitudinal Module of Stage D HF patients (21). Second, we administered IV treatment according to a standardized dosing protocol and were able to demonstrate similar effects in patients across a broad range of maintenance diuretic doses, including patients on mega doses exceeding 360 mg furosemide equivalents/day or the need for combination treatment with loop and thiazide diuretics. Finally, careful post-treatment laboratory surveillance permits a complete accounting of the safety of this treatment approach, including hypokalemia, worsening renal function, readmission rates, and mortality.

Another notable aspect of our cohort is the enrollment of patients across a broad spectrum of EF, including patients with HFpEF. The burden of HFpEF as a proportion of total HF is increasing, and these patients contribute a substantial proportion of HF hospitalizations (22). Nevertheless, the available therapies for these patients remain limited. Effective decongestion in HFpEF patients is frequently challenging due to comorbid renal disease, associated pulmonary hypertension, right ventricular dysfunction, and significant ventricular diastolic filling abnormalities that enhance sensitivity to abrupt changes in preload (23). Nonetheless, rates of worsening renal function and other adverse events were not different between HFpEF and HFrEF patients whom we treated. Accordingly, these data suggest that a protocolized approach to ambulatory IV diuresis may be a safe and effective route to relief of congestion without hospitalization for both patients with HFpEF and HFrEF.

In the absence of clear guidance from previous studies, our diuretic dosing strategy was adapted from the Diuretic Optimization Strategies Evaluation trial of

FIGURE 3 Efficacy Outcomes in Notable Subgroups

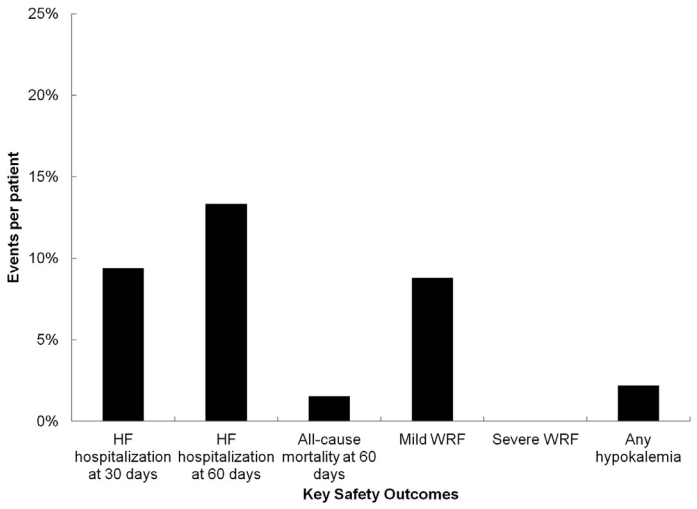


Weight loss was expressed in kilograms and urine output in liters. Outcomes were similar between patients with heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF). Successful decongestion was achieved in the majority of patients.

inpatients with acute decompensated HF (9). We applied stepped increases in IV loop diuretic doses for patients with higher maintenance dose requirements and combined bolus doses with a continuous infusion to maximize total diuretic dose over a short treatment duration. Although bolus diuretic dosing alone may have achieved comparable outcomes in some of the patients we enrolled, it is unclear whether this approach would have been sufficient to achieve effective diuresis for patients on higher maintenance doses of loop diuretics. Moreover, bolus dosing in the clinic setting is frequently inconvenient for HF patients, many of whom are elderly and may have difficulty managing diuretic-associated urinary urgency during the return commute home. We purposely monitor patients for up to 3 h to observe the initial response to diuretic administration, permit electrolyte repletion, and assess the need for incremental treatment with a second IV loop diuretic bolus dose or a supplemental thiazide diuretic. Although we provided in-unit cardiac telemetry, no clinically significant arrhythmias were noted during IV diuretic treatment, suggesting that this may not be critical. Treatment failure requiring hospitalization was rare, and all but 2 patients were successfully discharged to home after their initial treatment visit.

STUDY LIMITATIONS. Our analysis should be viewed in the context of certain limitations. This study was a small, single-center study at a tertiary HF center. Although we examined short-term outcomes in a selected population with more advanced HF symptoms, comparable efficacy of this strategy in the subset of patients with lower maintenance loop diuretic requirements suggests that this approach may be valid for a broad range of HF patients. Although we do not have details regarding oral diuretic titration before the clinic visit, previous data suggest that oral diuretic titration does not appear to affect the efficacy of ambulatory IV treatment (4). Furthermore, the high maintenance doses of loop diuretics and combination diuretic therapy in this population suggest that similar success would have been unachievable without IV therapy. Without a true control group, we cannot accurately assess the efficacy of the ambulatory IV treatment approach relative to standard HF care with regard to readmission prevention or mortality. We cannot exclude that some readmissions (particularly to other hospitals) may have been missed, although we made deliberate efforts through telephone interviews at 30 days and retrospective chart review to achieve complete accounting. Due to the number of hypothesis tests performed, chance alone may have accounted for the statistically significant differences in urine output and clinic weight loss observed between protocol groups. Finally, we cannot generalize the results from this hospital-based study to other practice settings; however, these data provide encouragement for further exploration of ambulatory alternatives to inpatient HF treatment, including home administration of IV diuretics or emergency department-based HF observation units.

FIGURE 4 Key Safety Outcomes



Selected key safety outcomes are depicted. Hypokalemia and transient worsening of renal function (WRF) occurred infrequently. Renal function returned to baseline in each patient. HF = heart failure.

CONCLUSIONS

In summary, our data suggest that ambulatory loop diuretic administration using a standardized protocol is effective in achieving decongestion in patients with decompensated HF across the spectrum of EF and maintenance diuretic doses. Many patients received repeat therapy, suggesting that this strategy may be an effective route to continuation of diuresis begun in the inpatient setting (as a strategy to reduce length of stay) or as an alternative to hospitalization for the management of hemodynamically stable patients with worsening HF symptoms and modest volume overload. In an increasingly resource-constrained environment, we believe that these data support the potential to reduce the need for hospitalization of stable HF patients at substantial cost savings with low-risk enhanced ambulatory HF treatment.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: An increasing number of patients with HF decompensation may be managed safely and effectively in the ambulatory setting. The use of a standardized protocol may be preferred in patients with advanced HF and high maintenance diuretic doses.

TRANSLATIONAL OUTLOOK 1: Short courses of IV diuretics may be used as an alternative to hospitalization for the management of HF decompensation. Comparative studies are warranted to identify patients who may benefit differentially from 1 strategy.

TRANSLATIONAL OUTLOOK 2: HF-related hospitalizations account for a significant financial burden on the health care system. Formal cost-analysis studies may determine the financial implications of ambulatory management compared with hospital management.

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KEY WORDS ambulatory treatment, heart failure, loop diuretics

APPENDIX For supplemental tables, please see the online version of this article.