Ambulatory Intravenous Diuretic Clinic Associated with Short-Term Risk Reduction in Mortality and Rehospitalizations in Patients Discharged with Heart Failure

AMY ST. AMAND, PharmD, BCPS; TRACEY H. TAVEIRA, PharmD, CDOE; KAITLIN E. HENTHORNE, PharmD; WEN-CHIH WU, MD, MPH

ABSTRACT

BACKGROUND: Data on effectiveness of ambulatory intravenous (IV) diuretic clinics for volume management in patients with heart failure to prevent rehospitalization and mortality are limited. Therefore, the primary goal of this research is to evaluate the effectiveness of an outpatient multidisciplinary IV diuretic clinic versus standard observational hospitalizations of less than 48 hours for decompensated heart failure on the time to rehospitalization or death.

METHODS: A retrospective cohort study of patients with heart failure (n=90) at the Providence Veterans Affairs Medical Center was conducted. Patients were included in the analyses if they received at least one ambulatory IV diuretic clinic visit or an observational hospitalization of less than 48 hours for decompensated heart failure between January 1, 2014 and June 30, 2016. Using Cox proportional hazards modeling, we compared the time to any hospitalization or death between the IV clinic and the observational hospitalization cohort over 180 days of follow-up.

RESULTS: In the ambulatory IV diuretic clinic group, 27 patients (mean age 78.3 ± 8.3 years) received a median of 3 (interquartile range [IQR] 2-12), IV diuretic treatments. In the comparison group, 63 patients (mean age 80.3 ± 11.0 years) were hospitalized for observation for 48 hours or less during the same time period. Adjusting for age and imbalances in baseline characteristics, left ventricular ejection fraction and enrollment in hospice care, the hazards of any hospitalization or death (HR 0.39, 95% confidence interval 0.19 to 0.83) were reduced for patients in the ambulatory IV diuretic clinic versus those in the observational hospitalization cohort.

CONCLUSIONS: In patients with decompensated heart failure, an ambulatory IV diuretic clinic was associated with risk reduction of any rehospitalization or death over 180 days of follow up when compared to a strategy of observational hospitalization for less than 48 hours. Future research should prospectively analyze outpatient IV therapy in a larger and more diverse population.

INTRODUCTION

An estimated 6.2 million Americans reported having a diagnosis of heart failure.[1] Heart failure accounts for 809,000 hospitalizations annually in the United States.[1] Approximately 21.4% of patients admitted to the hospital with a primary diagnosis of heart failure were readmitted within 30 days and 53.2% of patients were readmitted within 180 days of discharge.[2] More than half of these readmissions were determined to be preventable.[3]

Ambulatory intravenous (IV) diuretic clinics for volume management in patients with heart failure have been found safe and effective at promoting significant urine output,[4,5] weight loss[6] and improvement in dyspnea.[7] This strategy may provide an alternative to hospitalization for the management of heart failure patients. Data on the effectiveness of this strategy to prevent rehospitalization and mortality are limited, especially as compared to standard observational hospitalization care admissions. Therefore, the primary goal of this research is to evaluate the effectiveness of an outpatient multidisciplinary IV diuretic clinic versus standard observational hospitalizations of less than 48 hours for decompensated heart failure on the time to rehospitalization or death.

METHODS

Study Design

A retrospective analysis of consecutive patients treated for heart failure in either the ambulatory IV diuretic clinic or by way of an observational hospitalization of 48 hours or less at the Providence Veterans Affairs (VA) Medical Center between January 1, 2014 and October 1, 2016 was conducted.

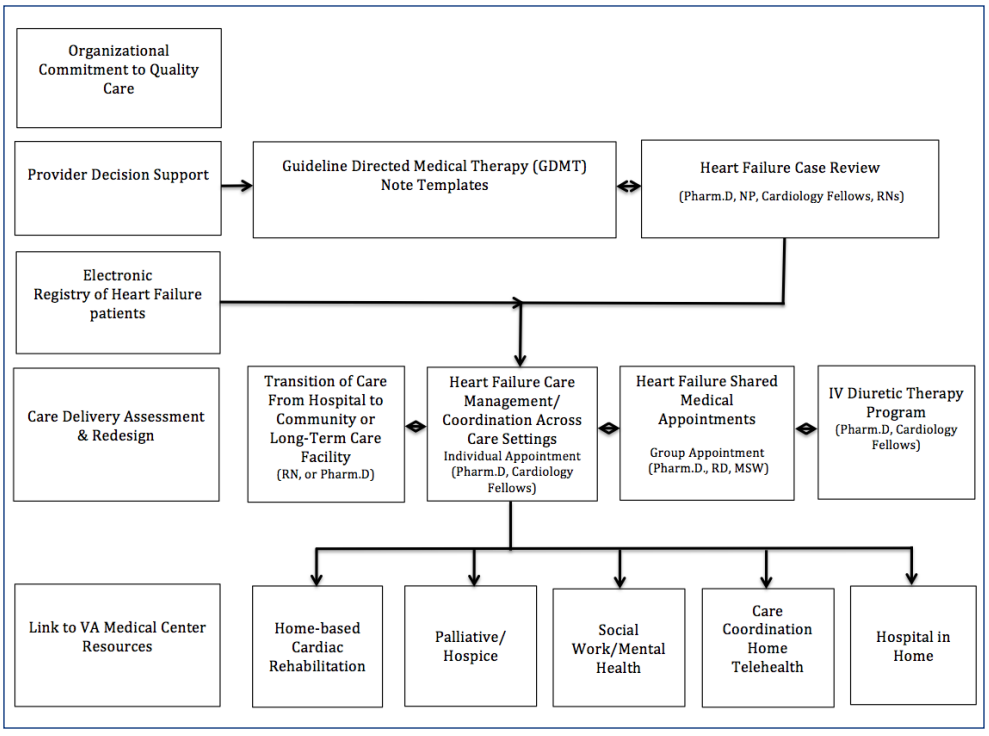
Study Patients

Patients were included in the analyses if they were previously discharged from the Providence VA Medical Center with a primary diagnosis of decompensated heart failure and had a least one treatment in the ambulatory IV diuretic clinic or were re-admitted for a less than 48 hours observation period for treatment of decompensated heart failure after their heart failure discharge. Time "0" was set at the moment the patient required one of the two interventions (IV diuretic clinic or observational hospitalization of <48 hours). Each patient was followed for 180 days since the moment they received the intervention.

Setting

The organization of the heart failure care program at the Providence Veterans Affairs Medical Center is shown in **Figure 1**. The goal of the heart failure care program is to improve health status and to decrease hospitalizations and death for patients with an established history of heart failure. The heart failure care team was designed using the tenets of the chronic care model and is comprised of a cardiologist, cardiology fellows, nurse practitioners, registered nurses and clinical pharmacists who provide medication optimization, self-management education, disease state monitoring and care coordination.[8] As per local VA policy all patients who were hospitalized with a primary diagnosis of heart failure were referred to the heart failure care program by cardiology or the inpatient treatment team. Prior to discharge the patient would receive an inpatient transition of care appointment by either the heart failure nurse or clinical pharmacist trained in heart failure care management. The transition of care appointment consisted of brief heart failure education and medication reconciliation. An appointment in either the individual heart failure care program, shared medical appointment group program or outpatient IV diuretic program would be scheduled depending upon the individual patient's needs. Patients who were assigned to receive heart failure care management in the individual clinic received a 30-minute face to face appointment with a clinical pharmacist or cardiology fellow if they refused to be seen in a group setting or did require immediate post-discharge diuresis. Each visit included patient education, behavioral modification, disease state monitoring and medication optimization. The shared medical appointment program consisted of 2-hour group sessions that met weekly for 4 weeks.[9] The first half of each session focused on self-management education provided by a nurse, registered dietician, social worker or clinical pharmacist. During the second half of each session the clinical pharmacist performed a brief physical exam to assess volume status and provided medication optimization. The ambulatory IV diuretic was staffed by cardiology fellows or a clinical pharmacist and provided an alternative to inpatient admission for IV diuretic therapy for patients with mild to moderate decompensated heart failure. Patients could also be referred to the IV diuretic clinic from the individual heart failure clinic appointment or the heart failure shared medical appointment program at the discretion of the heart failure provider. The frequency of outpatient IV diuretic treatment was determined at the discretion of the treating provider but was generally held once weekly. Providers in the heart failure individual clinic, heart failure shared medical group appointment program and IV diuretic program also provided care coordination and referred patients to home-based cardiac rehabilitation, palliative or hospice care, social work or mental health, home telehealth monitoring or the hospital in-home program on an as needed basis.

Figure 1. Heart Failure Program Overview



Interventions

Ambulatory IV diuretic clinic: Patients in the IV diuresis cohort received IV loop diuretics for hypervolemia in the outpatient setting. As per the Providence VA Medical Center's protocol, the following items were assessed: vital signs, weight, EKG, laboratory values (basic metabolic panel, heparinized potassium, brain natriuretic peptide (BNP), digoxin levels [if indicated], and magnesium levels). Urine output was recorded hourly and upon the conclusion of IV diuresis therapy. Referral to self-care education, advanced care planning and palliative care were made when applicable.

Observation admission cohort: The observation admission cohort received an evaluation and initial treatment for hypervolemia in the emergency room followed by an inpatient hospitalization of less than 48 hours in duration as per the discretion of the treating emergency

room physician. Emergency room physicians did not have the ability to directly refer to the ambulatory IV diuretic clinic but could refer to the heart failure clinic program for further follow-up and subsequent diuresis.

End Points

Electronic medical records were reviewed for patient outcomes. The primary endpoint was the time to all-cause rehospitalization or death. The secondary endpoint was the time to heart failure rehospitalization or death.

Covariates

Patient demographics, comorbidities and laboratory values were also abstracted from the electronic medical record. Patients were considered to have a history of hypertension, hyperlipidemia, chronic obstructive pulmonary disease, pulmonary hypertension, atrial fibrillation, type 2 diabetes mellitus, obstructive sleep apnea, or stroke if it was documented in the medical record prior to the index event or the patients were receiving active treatment specific for the disease states. Patients were considered to have a history of coronary artery disease if they had documented evidence of a myocardial infarction, prior cardiac stent, or a prior cardiovascular bypass graph. Blood pressure, heart rate and body mass index (BMI), BNP, estimated glomerular filtration rate (eGFR) and potassium and serum creatinine values were abstracted upon presentation to the initial index event and again within seven days post completion or discharge. Patients were considered to be current users if active tobacco use was documented during the index event encounter. The most recent low-density lipid profile level prior to the patients index event was abstracted for the analysis. Antihypertensive medication use was ascertained at the initial ambulatory care IV diuretic visit or upon presentation for an observational hospitalization admission. Antihypertensive medications were categorized into the following classes: angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, β-adrenergic blockers, calcium channel blockers, thiazide diuretics, loop diuretics, and potassium sparing diuretics.

Statistical Analysis

The baseline characteristics of patients who were seen in the ambulatory IV diuresis clinic and those admitted for an observational heart failure hospitalization of less than 48 hours were compared using a t test for continuous variables and Chi-square test for categorical variables. Cox proportional hazards modeling was used to compare the time to all-cause rehospitalization or death and the time to heart failure rehospitalization or death adjusting for variables imbalanced at baseline (BMI, obstructive sleep apnea, COPD, use of loop diuretics), as well as, age, eGFR, left ventricular ejection fraction (LVEF), and hospice enrollment. Our result model had adequate discrimination and calibration for the study population (Harrell C=0.62). Kaplan-Meier curves were used to estimate freedom of hospitalization or death between the two cohort arms. We tested the proportionality of hazards assumptions for the Kaplan-Meier curves by visual inspection and analysis of the Schoenfeld residuals.[10] The proportional hazards assumption was confirmed for the primary analysis (P=0.39).

RESULTS

Between January 1, 2014 and June 30, 2016, 167 patients were discharged from the Providence VA Medical Center with a primary diagnosis of decompensated heart failure. Of those patients, 77 were excluded from our analyses because they did not receive a follow-up treatment in either the outpatient IV diuretic clinic or an observational hospitalization of <48 hours. A total of 27 unique patients received a median of 3 interquartile range (IQR 2–12) diuretic treatments in the ambulatory IV diuretic program. The median total urine output for those treated in the ambulatory IV diuretic clinic was 2525.0 mL (IQR 1075-9830mL). Over the same time period 63 patients were admitted for an observational hospitalization of <48 hours with a primary diagnosis of decompensated heart failure (**Figure 2**). Seven of the patients in the observational hospitalization of <48 hours cohort were subsequently referred by a heart failure clinic providers to receive ambulatory IV diuretic treatment and received an average of 12.3 ± 12.1 treatments over the 180 days of follow-up.

Baseline characteristics were similar between the two cohorts; however, patients in the observational admission of <48 hours group tended to be older, had significantly lower BMI levels and were less likely to have a diagnosis of chronic obstructive pulmonary disease (COPD) or Obstructive Sleep Apnea (**Table 1**).

When compared to those patients in the observational admission cohort, those patients in the ambulatory IV diuretic cohort had a lower unadjusted hazard ratio of

Figure 2. Consort Study Flow Diagram

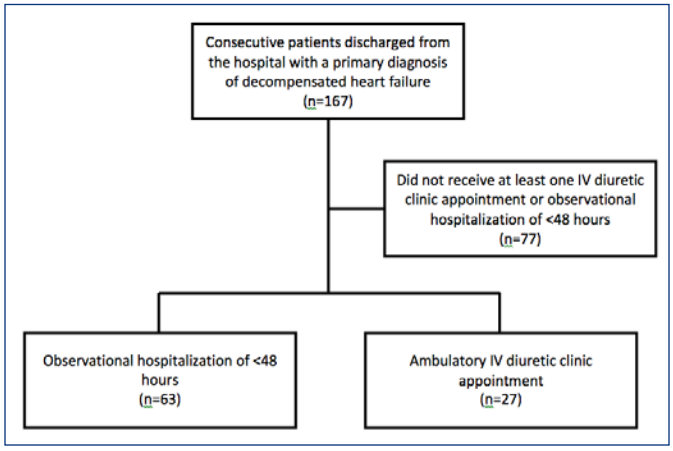


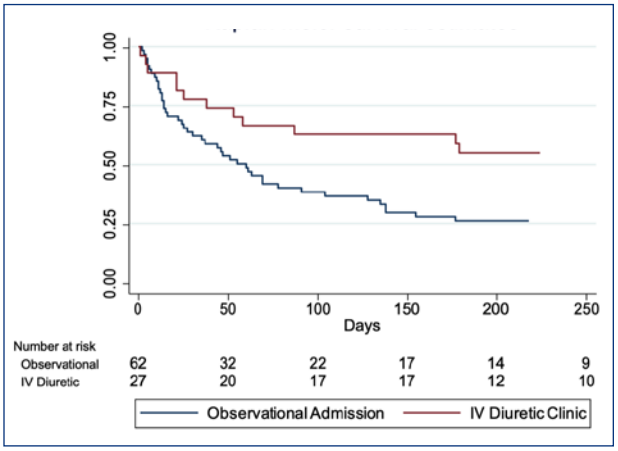
Table 1. Baseline Characteristics

	Admitted for Observation (n = 63)	IV Diuresis (n = 27)	P value
Age (years)	80.3 ± 11.0	78.3 ± 8.3	0.40
Male Sex, n (%)	61 (96.8)	27 (100.0)	0.35
Caucasian, n (%)	60 (95.2)	27 (100.0)	0.25
Ejection Fraction at Discharge (%)	45.4 ± 14.2	46.1 ± 12.7	0.82
HFrEF, n (%)	18 (28.6)	10 (37.0)	0.43
Coronary Artery Disease, n (%)	49 (77.8)	22 (81.5)	0.69
COPD, n (%)	18 (28.6)	14 (51.9)	0.03
Atrial Fibrillation, n (%)	44 (69.8)	17 (63.0)	0.52
Type 2 Diabetes Mellitus, n (%)	32 (50.8)	15 (55.6)	0.68
Obstructive Sleep Apnea, n (%)	16 (25.4)	16 (59.3)	<0.01
Pulmonary Hypertension (%)	10 (15.9)	9 (33.3)	0.06
Hypertension, n (%)	58 (92.1)	25 (92.6)	0.93
Hyperlipidemia, n (%)	56 (88.9)	24 (88.9)	1.00
Depression, n (%)	20 (31.8)	16 (59.3)	0.02
Current Tobacco User, n (%)	7(11.1)	4(14.8)	0.62
BMI (kg/m2)	28.8 ± 5.7	32.6 ± 7.9	0.01
Systolic Blood Pressure (mmHg)	126.3 ± 20.9	120.1 ± 19.7	0.19
Diastolic Blood Pressure (mmHg)	70.0 ± 10.2	66.7 ± 10.8	0.17
Low Density Lipoprotein (mg/dL)[a]	84.1 ± 34.6	78.0 ± 19.7	0.41
eGFR (mL/min/1.73m2)	49.5 ± 22.7	40.3 ± 15.7	0.06
Serum Creatinine at Discharge	1.7 ± 1.0	2.1 ± 1.4	0.21
BNP(pg/mL)	965.7 ± 814.5	664.7 ± 940.5	0.13
Hospice, n (%)	10 (15.9)	3 (11.1)	0.56
ACEi or ARB, n (%)	39 (61.9)	15 (55.6)	0.57
Beta Blockers, n (%)	(82.5)	23 (85.2)	0.76
Loop Diuretics, n (%)	49 (77.8)	26 (96.3)	0.03
Calcium Channel Blocker, n (%)	17 (27.0)	5 (18.5)	0.39
Spironolactone, n (%)	6 (9.5)	4 (14.8)	0.46
Isosorbide Mononitrate, n (%)	8 (12.7)	5 (18.5)	0.47
Hydralazine, n (%)	5 (7.9)	4 (14.8)	0.32
Thiazide Diuretic, n (%)	3 (3.5)	4 (14.8)	0.10
Statin, n (%)	49 (77.8)	23 (85.2)	0.42
Fish Oil, n (%)	3 (4.8)	0	0.25
Aspirin, n (%)	50 (79.4)	20 (74.1)	0.58
Warfarin, n (%)	21 (33.3)	8 (29.6)	0.73
Direct Oral Anticoagulants, n (%)	3 (4.8)	1 (3.7)	0.82
Antiarrhythmic, n (%)	4 (6.40	1 (3.7)	0.62
Digoxin, n (%)	3 (4.76)	2 (7.4)	0.62
Magnesium Oxide, n (%)	1 (1.6)	3 (11.1)	0.05

All values expressed as mean ± standard deviation unless indicated otherwise
a = (n=58 Observation, n=25 IV Diuretic Clinic)

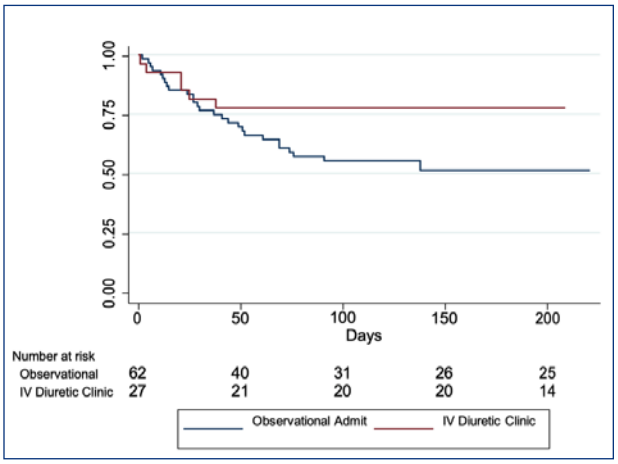
any-rehospitalization or death 0.43 (95%CI 0.23–0.81). After adjustment for age, BMI, diagnosis of OSA, COPD, eGFR, loop diuretic use, LVEF, and hospice enrollment, the adjusted hazard ratio for any rehospitalization or death was 0.43, 95% CI (0.21–0.88) for those who received treatment in the ambulatory IV diuretic therapy as compared to those in the observational admission cohort. **Figure 3** shows the unadjusted Kaplan-Meier survival curves of those in the observational admission cohort and the ambulatory IV diuretic therapy cohorts over 180 days of follow-up. The median number of days to any rehospitalization or death was 38.0, (IQR 21–87 days) for those who received ambulatory IV diuretic therapy as compared with a median of

Figure 3. Kaplan-Meir Survival Curves for Time to All Cause Rehospitalization or Death



Kaplan-Meier curves showing the proportion of individuals without all cause hospital readmission or death over 180 days of follow-up (red curve = Ambulatory IV Diuretic Clinic; blue curve = Observational Admission <48h).

Figure 4. Kaplan-Meir Survival Curves for Time to Heart Failure Rehospitalization or Death



Kaplan-Meier curves showing the proportion of individuals without heart failure hospital readmission or death over 180 days of follow-up (red curve = Ambulatory IV Diuretic Clinic; blue curve = Observational Admission <48h).

27, (IQR 11–68 days) for those in the observational admission cohort. A total of 4 (6.4%) patients in the observational cohort and 2 (7.4%) from the IV diuretic therapy clinic died during the 180 days of follow-up, (p=0.85).

There was also a significant improvement in the risk of heart failure rehospitalization or death, adjusted HR 0.32 (95% CI 0.12–0.84) (**Figure 4**).

DISCUSSION

In patients with mild to moderate decompensated heart failure within the 6-month follow-up period of their previous heart failure hospital discharge, ambulatory IV diuretic clinic was associated with a reduced risk of all cause rehospitalization, heart failure hospitalization or death over 180 days of follow-up when compared to patients who had an observational hospitalization of 48 hours or less during the same time period.

This finding is important because beginning on October 1, 2012, Section 3025 of the Affordable Care Act added section 1886(q) to the Social Security Act establishing the Hospital Readmissions Reduction Program (HRRP). The HRRP requires the Centers for Medicare and Medicaid Services (CMS) to reduce payments to Inpatient Prospective Payment System (IPPS) hospitals with excess heart failure readmissions.[11] Thus, the American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines added a Class I recommendation to utilize multidisciplinary heart failure disease management programs to facilitate implementation of guideline-directed medical therapy, to address barriers to behavioral modification, and to reduce the risk of subsequent rehospitalization for HF for patients at high risk of hospital readmissions.[12]

This work builds on a limited number of studies evaluating the safety and effectiveness of outpatient IV diuretic programs demonstrating symptomatic improvements in dyspnea, hypervolemia with low to non-existent rates of serious adverse events and has the potential to reduce hospitalizations.[4,5,13] Priors studies demonstrating safety and reduction of rehospitalizations utilized board certified cardiologists to perform IV medication managment.[5,13] However, our study is unique in that the providers of the outpatient IV diuretic treatment team could be comprised of a physician, a nurse practitioner or a clinical pharmacist trained in heart failure care management interchangeably to provide IV therapy medication treatments.

There has been a push to provide novel treatment strategies of more complex patients to the ambulatory care setting. The clinical implications of the present study demonstrates the feasibility and safety of a multidisciplinary care providers to prescribe intravenous diuretic therapy and is an attractive alternative to emergency department utilization or observational hospitalizations for patients with mild to moderate decompensated heart failure. It opens up possibilities of different setting for IV diuretic clinic depending on institutional needs. The current study setting is within the outpatient oncology infusion center of the hospital. Possibilities exist for the IV therapy to be provided in a completely outpatient clinic setting or a carved-out section of an emergency room, similar to a "chest pain unit."

There are several limitations to this study. The basic assumption of the current study is that patients who required IV diuretic therapy were similar in disease severity whether they were seen in the ambulatory IV diuretic clinic or hospitalized for 48h observation. The results remained significant despite adjustments for age, BMI and COPD which were different at baseline. However, given the retrospective nature of this study, patients were not randomly allocated to the treatment interventions for which the possibility of residual confounding exists and alternative explanation to study findings cannot be excluded.

The intervention took place at a single center within the Veterans Health Administration and the absolute number of patients is small and relatively homogenous (mostly men). Additionally, heart failure hospitalization information was unavailable for private payer non-VA admissions unless records were forwarded by a non-VA provider. Therefore, it is possible that not all hospitalizations occurring outside of the Veterans Health Administration were fully captured in our data.

CONCLUSIONS

In patients with mild to moderate decompensated heart failure, ambulatory IV diuretic clinic was associated with risk reduction of any rehospitalization or death over 180 days of follow-up when compared to a strategy of observational hospitalization for less than 48 hours. However, future research should prospectively analyze outpatient IV therapy in a larger and more diverse population.

References

1. Virani SS, Alonso A, Benjamin EJ, et al. Heart Disease and Stroke Statistics-2020 Update: A Report From the American Heart Association. *Circulation*. Mar 2020;141(9):e139-e596. doi:10.1161/CIR.0000000000000757
2. Elkaryoni, A, Enriquez J. Early and Late Readmission Rates for Heart Failure Hospitalizations in Patients With Preserved and Reduced Ejection Fraction: Insights From the Nationwide Readmission Database 2010-2016. *Circulation*. 2019;140(Suppl 1)(1):A10796.
3. Ogbemudia EJ, Asekhame J. Rehospitalization for heart failure in the elderly. *Saudi Med J*. Oct 2016;37(10):1144-7. doi:10.15537/smj.2016.10.15259
4. Buckley LF, Carter DM, Matta L, et al. Intravenous Diuretic Therapy for the Management of Heart Failure and Volume Overload in a Multidisciplinary Outpatient Unit. *JACC Heart Fail*. Jan 2016;4(1):1-8. doi:10.1016/j.jchf.2015.06.017
5. Makadia S, Simmons T, Augustine S, et al. The diuresis clinic: a new paradigm for the treatment of mild decompensated heart failure. *Am J Med*. May 2015;128(5):527-31. doi:10.1016/j.amjmed.2014.11.028

6. Banerjee P, Tanner G, Williams L. Intravenous diuretic day-care treatment for patients with heart failure. *Clin Med (Lond)*. Apr 2012;12(2):133-6. doi:10.7861/clinmedicine.12-2-133
7. Lazkani M, Ota KS. The role of outpatient intravenous diuretic therapy in a transitional care program for patients with heart failure: a case series. *J Clin Med Res*. Dec 2012;4(6):434-8. doi:10.4021/jocmr1106w
8. Bodenheimer T, Wagner EH, Grumbach K. Improving primary care for patients with chronic illness. *JAMA*. Oct 2002;288(14):1775-9. doi:10.1001/jama.288.14.1775
9. Wu WC, Parent M, Dev S, et al. Group medical visits after heart failure hospitalization: Study protocol for a randomized-controlled trial. *Contemp Clin Trials*. 08 2018;71:140-145. doi:10.1016/j.cct.2018.06.015
10. Schoenfeld D. Partial residuals for the proportional hazards regression model. *Biometrika*. 1982;69(1):239-241
11. Services CfMaM. Hospital Readmissions Reduction Program (HRRP). Accessed September 23, 2020.
12. Buckley LF, Seoane-Vazquez E, Cheng JW, et al. Comparison of Ambulatory, High-Dose, Intravenous Diuretic Therapy to Standard Hospitalization and Diuretic Therapy for Treatment of Acute Decompensated Heart Failure. *Am J Cardiol*. Nov 2016;118(9):1350-1355. doi:10.1016/j.amjcard.2016.07.068
13. Zuzarte P, Kostiw K, Maciukiewicz M, Figueira ML, Costa-Vitali A. Outpatient disease management program for heart failure: a multidisciplinary approach with an intravenous diuretic therapy. *INSUFICIENCIA CARDIACA*. 2018;13:2-9.

Authors

Amy St. Amand, PharmD, BCPS, Providence Veterans Affairs Medical Center, Providence, RI; University of Rhode Island College of Pharmacy, Kingston, RI.

Tracey H. Taveira, PharmD, CDOE, Providence Veterans Affairs Medical Center, Providence, RI; Department of Medicine, Alpert Medical School of Brown University, Providence, RI.

Kaitlin E. Henthorne, PharmD, Pen Bay Medical Center, Rockport, ME.

Wen-Chih Wu, MD, MPH, Providence Veterans Affairs Medical Center, Providence, RI; Department of Medicine, Alpert Medical School of Brown University, Providence, RI; Department of Epidemiology, Brown University School of Public Health, Providence, RI; Cardiovascular Wellness and Prevention Center at Lifespan, Providence, RI.

Disclosures

Funding: Wen-Chih Wu, MD, MPH, was supported by the VA HSRD grant 5I01HX001800-005. The views expressed in this publication represent that of the authors and not of the Department of Veterans Affairs.

Conflicts: The authors declare no conflicts of interest.

Correspondence

Tracey H. Taveira, PharmD, CDOE
Professor of Pharmacy
University of Rhode Island College of Pharmacy
Avedisian Hall
7 Greenhouse Road
Kingston, RI 02881