Inpatient versus outpatient intravenous diuresis for the acute exacerbation of chronic heart failure

Ilia G. Halatchev a,b,⇑, Wen-Chin Wu c,d, Paul A. Heidenreich e, Elma Djukic a, Sumitra Balasubramanian f, Kelly B. Ohlms f, Jay R. McDonald a,b

a Veterans Affairs St. Louis Health Care System, John Cochran Division, St. Louis, MO, United States
b Washington University School of Medicine, St. Louis, MO, United States
c Veterans Affairs Providence Health Care System, Providence Medical Center, Providence, Rhode Island, United States
d Warren Alpert Medical School, Brown University, Providence, Rhode Island, United States
e Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, United States
f Clinical Research and Epidemiology Workgroup at Veterans Affairs St. Louis Health Care System, John Cochran Division, St. Louis, MO, United States

Article info
Article history:
Received 9 June 2021
Received in revised form 12 August 2021
Accepted 14 August 2021

Keywords:
Heart failure
Outcomes
Diuresis
Acute decompensated heart failure
Emergency department

Abstract
Background: We established an IV outpatient diuresis (IVOiD) clinic and conducted a quality improvement project to evaluate safety, effectiveness and costs associated with outpatient versus inpatient diuresis for patients presenting with acute decompensated heart failure (ADHF) to the emergency department (ED).

Methods: Patients who were clinically diagnosed with ADHF in the ED, but did not have high-risk features, were either diuresed in the hospital or in the outpatient IVOiD clinic. The dose of IV diuretic was based on their home maintenance diuretic dose. The outcomes measured were the effects of diuresis (urine output, weight, hemodynamic and laboratory abnormalities), 30–90 day readmissions, 30–90 day death and costs.

Results: In total, 36 patients (22 inpatients and 14 outpatients) were studied. There were no significant differences in the baseline demographics between groups. The average inpatient stay was six days and the average IVOiD clinic days were 1.2. There was no significant difference in diuresis per day of treatment (1159 vs. 944 ml, p = 0.46). There was no significant difference in adverse outcomes, 30–90 day readmissions or 30–90 day deaths. There was a significantly lower cost in the IVOiD group compared to the inpatient group ($839.4 vs. $9895.7, p=<0.001).

Conclusions: Outpatient IVOiD clinic diuresis may be a viable alternative to accepted clinical practice of inpatient diuresis for ADHF. Further studies are needed to validate this in a larger cohort and in different sites.

Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

The prevalence of heart failure (HF) in the United States is estimated to be rising to >5.7 million people [1]. Because of rising prevalence and costs, HF accounts for 40 billion dollars in indirect and direct healthcare costs annually [2]. ADHF hospitalizations are associated with increased risk of recurrent hospitalization and 1-year mortality of nearly 30% [3,4], likely driven by a subset of high risk patients [5–8]. Eighty percent of patients with ADHF present to the emergency department (ED) [9], and 91.5% of these are admitted to the hospital. This paradigm has not changed for the past 50 years and is a major public health problem [10], as it is the leading cause of hospitalizations for patients > 65 years of age [11], with costs estimated at 11 billion dollars annually [9].

A potential reason for this pervasive paradigm is that The American College of Cardiology and American Heart Association (ACC) (AHA) guidelines [12] list several factors that are associated with poor outcomes in patients presenting with ADHF, but because of a paucity of published data, do not provide guidance on appropriate location (home, inpatient ward or intensive care unit) for therapy. The guidelines instead focus on guiding therapy in the typical location of ADHF – the hospital – with the mainstay being intravenous (IV) diuresis and discharge planning. To date, there are several studies that have evaluated the efficacy and safety of
outpatient IV diuresis for congested HF patients [13–17] who were identified in the outpatient clinics. They showed that IV furosemide administration was effective in diuresing outpatients and that it was safe, even at 200 mg bolus doses. These studies, however, did not directly compare the feasibility, safety, or costs of inpatient versus outpatient IV furosemide decongestion of ADHF patients presenting to the ED.

We established an IV outpatient diuresis (IVOiD) clinic at a Veterans Health Administration (VHA) hospital, and conducted a quality improvement project to evaluate the safety, efficacy and cost associated with outpatient IV diuresis for patients in the ED with ADHF and who would have otherwise been admitted.

2. Methods

This is prospective open-label pilot quality improvement (QI) project was approved by the VHA hospital’s QI/quality assurance (QA) board and research department. The data storage, analysis and publication were approved by the Institutional Review Board (IRB) for an exemption.

2.1. Patient identification

Patients presenting to the ED with dyspnea, shortness of breath, difficulty breathing, cough, breathlessness, orthopnea, paroxysmal nocturnal dyspnea, swelling and/or edema were identified as potentially having ADHF. After initial identification, patients were further evaluated to confirm ADHF by the following checklist and decision tree (Fig. 1):

1. Previously documented diagnosis of CHF

2. High likelihood of ADHF based on clinical assessment, using a modified Framingham Study criteria [18], with presence of either: (i) one sign or symptom and one laboratory or imaging finding or (ii) one symptom and one sign:
   a. Symptoms
      i. Worsening dyspnea
   b. Signs
      i. Increased lower extremity edema
      ii. Unintentional weight gain ≥ 5 lb
   c. Laboratory or imaging findings
      i. Pulmonary congestion and/or pleural effusions by chest x-ray
      ii. B-type natriuretic peptide (BNP) level which is above euvolemic baseline
      iii. Increased internal jugular venous distention (JVD)
      iv. Increased abdominal swelling or ascites

Further, patients were excluded if they had had one or more of the following high-risk findings:

1. Suspicion or diagnosis of acute coronary syndrome by history, physical, laboratory or imaging data

---

Fig. 1. Inpatient versus outpatient intravenous diuresis flow diagram. Patients presenting to the emergency department were initially screened for acute decompensated heart failure. Those with heart failure exacerbation were further screened for high risk features; if not present, the emergency department practitioner decided if they would be admitted or discharged to follow-up in the IVOiD clinic. Patients who had worsening symptoms or not responding to outpatient diuresis were directly admitted to the hospital. ED: emergency department; MI: myocardial infraction; PE: pulmonary embolus; HF: heart failure; IVOiD: intravenous outpatient diuresis clinic; Cr: creatinine; eGFR: estimated glomerular filtration rate.
2. Suspicion or diagnosis of acute pulmonary embolus by history, physical, laboratory or imaging data
3. Systolic blood pressure (SBP) < 100 mmHg or heart rate (HR) > 100 beats per minute
4. Presence of new hypoxia as defined by O2 saturations < 91% on room air or on chronic stable O2 requirement that requires (additional) supplemental oxygen or tachypnea with respiratory rate > 30 breaths/minute
5. Presence of a new sustained arrhythmia with HR > 100, such as atrial flutter, atrial fibrillation, atrial or ventricular tachycardia
6. New diagnosis of HF
7. Creatinine elevation ≥ 25% from baseline or severe renal dysfunction as defined by eGFR < 20 ml/min/1.73 m²
8. Electrolyte abnormalities with serum sodium ≤ 127 or ≥ 141 mmol/L or potassium ≤ 3.2 or ≥ 5.5 mmol/L
9. New or chronic intravenous inotrope requirement
10. Previously known or newly diagnosed constrictive pericarditis, infiltrative cardiomyopathy or tamponade
11. Inability to travel to the hospital on a daily basis due to transportation issues
12. Other non-HF comorbidities requiring inpatient admission

ADHF patients without high-risk features with a plan to be admitted were discussed with the ED practitioner; the practitioner was given an option to either proceed with inpatient admission vs. discharge to follow up in the outpatient IVOiD clinic. Patients admitted to the hospital for IV diuresis received standard of care, which was decided by the primary medicine team. Cardiology was consulted at the discretion of the primary team.

2.2 Inpatient ADHF management

Patients admitted to the hospital for IV diuresis received standard of care, which was decided by the primary medicine team. Cardiology was consulted at the discretion of the primary team.

2.3 IVOiD clinic protocol: Timeline, medication dosing, and monitoring

2.3.1 Timeline

Patients discharged from ED for outpatient diuresis were instructed to present to IVOiD clinic the subsequent day.

- The patient was monitored for symptoms, vital signs, rhythm disturbances, fluid intake, and urine output (T – 1:30–7:00);
- Blood was drawn for BMP, BNP and Mg, at the end of diuresis and prior to discharge (T – 7:00).

If a patient did not present on a day of IVOiD clinic they received a phone call and rescheduled for the following business day.

2.3.2 Medication and dosing

Dosing of furosemide, metolazone and KCl was based on a study by Buckley et al. 14, whereby:

- Patients without maintenance dose of furosemide, or patients only on hydrochlorothiazide or spironolactone, received an IV bolus of furosemide 40 mg and oral dose (PO) dose of KCl 40 mEq.
- Patients on low-to-moderate home maintenance dose of diuretic, defined as presenting home furosemide (or equivalent; oral furosemide 40 mg = intravenous furosemide 20 mg = torsemide 20 mg = bumetanide 1 mg) > 0 and ≤ 160 mg total 24 hr dose, received an IV bolus of furosemide 1.5 times their 24 hr total home maintenance dose, and a PO dose of KCl 60 mEq.
- Patients on high-dose home maintenance dose of diuretic, defined as presenting home furosemide (or equivalent) > 160 mg total 24 hr dose, received pretreatment with a PO dose of metolazone 5 mg and PO dose of KCl 40 mEq 30 min prior to IV bolus of furosemide 240 mg and a repeat PO dose of KCl 40 mEq 4 hr after furosemide IV administration.
- Potassium was supplemented on discharge from the IVOiD clinic based on changes observed with IV diuresis, such that if potassium decreased by ≥ 0.4 mmol/L, patient’s KCl supplementation was increased by 40 mEq per day or was started on 40 mEq of KCl daily if previously not on potassium supplementation.

2.3.3 Monitoring

Vital signs were measured every 30 min from presentation to discharge and a practitioner was alerted if any of them reached parameters as per exclusion criteria above. All patients were monitored on telemetry, and a practitioner was notified for any non-sustained or sustained arrhythmias. Fluid intake and urine output were recorded every 30 min after administration of IV Furosemide until patient was discharged from the IVOiD clinic. Patients’ weight was measured on presentation and at time of clinic discharge.

2.4 Post-IVOiD clinic diuretic dose adjustment and follow up

Follow-up after outpatient diuresis (in either IVOiD clinic for additional IV diuretics or HF clinic) and home diuretic dosing adjustment decision was based on an estimated “dry weight” (which was defined as the nadir weight for the past year that was associated with lowest recorded BNP, the least prominent HF symptoms, and/or lowest JVD):

- Patients were instructed to return to IVOiD clinic on following workday if at the time of IVOiD discharge their weight was ≥ 5 lb above baseline “dry weight” and/or JVD of ≥ 12 cm of H2O. They were also instructed to increase their home dose of diuretic by 2-fold for the rest of the day.
- Patients were instructed to continue with the 2-fold increased home dose of oral diuretics if at the time of IVOiD discharge, their weight was < 5 lb above baseline “dry weight” and/or JVD of ≤ 12 cm H2O until they reach their estimated “dry weight”, at which point to return back to baseline diuretic dose.
I.G. Halatchev, Wen-Chin Wu, P.A. Heidenreich et al. IJC Heart & Vasculature 36 (2021) 100860

Patients were instructed to continue with their prior home dose of diuretic if at “dry weight” and/or JVD ≤ 8 cm.

All patients were instructed to and scheduled for follow up in HF clinic in 1 week and to have repeat Basic Metabolic Panel (BMP)/BNP/Mg in ≤ 1 week.

2.5. Data collection and comparisons

IRB approved data collection through chart review in the Computerized Patient Records System (CPRS) and from data collected in the IVOId clinic. Patient identifiers were removed and data stored in a secure VA server in a Microsoft Excel spreadsheet. We compared the patients’ baseline characteristics and outcomes, including the effects of diuresis (urine output, weight, hemodynamic and laboratory abnormalities), 30–90 day readmissions, 30–90 day death and costs between the inpatient and IVOId clinic groups.

2.5.1. Patient baseline data collection

Baseline data included: presenting ER visit date, age, gender, ethnicity, vital signs, weight, NYHA class, left ventricular ejection fraction, baseline-furosemide equivalent dose, cardiac medications, laboratory values (sodium, potassium, blood urea nitrogen (BUN), creatinine and BNP), and comorbidities (coronary artery disease, atrial fibrillation, chronic kidney disease, diabetes mellitus, chronic obstructive pulmonary disease, implantable defibrillator or cardiac resynchronization therapy device). Inpatient length of stay and number of IVOId clinic visits per patient were recorded. Treatment parameters were recorded: number and amount of IV furosemide equivalent doses, blood pressure and heart rate 90 min after diuretic administration, fluid intake and output for each 24 h for inpatients and after IV furosemide administration for IVOId patients, the change in weight at the time of discharge, potassium, BUN and creatinine after furosemide administration.

2.5.2. Cost data collection

Healthcare delivery costs were collected retrospectively for each patient from the St. Louis VA Managerial Cost Accounting System. For IVOId clinic patients, costs collected included all encounters associated with: cardiology clinic visit (cardiology provider evaluation and recommendations), laboratories on the day of IVOId clinic, pharmacy costs, any non-cardiology consultations and telephone follow up. The IVOId costs for clinic space use, equipment uses, and nursing time were not collected as the clinic was built to be part of the daily clinical/patient care workflow and operations of the cardiac catheterization and echocardiography labs. For patients admitted to the hospital costs collected included all encounters associated with: room and bed, food production and delivery, inpatient internal medicine management, inpatient transportation, consultative services (cardiology consultation, palliative care consultation, physical therapy, occupational therapy, dietary consultation, respiratory therapy, social work, chaplain services, wound care, prosthetics), pharmacy/medications, laboratory testing, imaging, and administrative.

2.6. Analysis and statistics

All analyses were performed using Statistical Analytical System (SAS) software version 9.4 (SAS Institute, Cary, NC). Continuous variables data was analyzed as mean and standard deviations. Categorical and nominal data was analyzed as frequencies and percentages. Bimodal data was analyzed as median and interquartile ranges. A Student’s t-test was used for continuous variables and chi-square for categorical data. Survival analysis was performed using Kaplan–Meier estimator. A 2-sided p-value of 0.05 or less was considered significant.

3. Results

Thirty-six patients met inclusion criteria. Of these, 22 were treated inpatient, and 14 treated outpatient.

3.1. Baseline characteristics and diuretic administration

There were no significant differences between the inpatient and outpatient patient baseline characteristics (Table 1). The majority were male with nearly equal distribution of Caucasians and African-Americans. The two groups had median left ventricular ejection fractions of 40% and similar: (i) symptoms: predominantly NYHA functional class III, (ii) HF associated comorbidities and therapies, (iii) mean baseline furosemide equivalent dose of loop diuretic of 80 mg per day, (iv) median baseline Cr of 1.5 mg/dL, and (v) BNP of 900 pg/mL. Median inpatient length of stay was 6 days as compared to median of 1 outpatient IVOId clinic visit (Table 2). Eleven of the 14 IVOId outpatients were diuresed with IV diuretic once and 3 were diuresed twice. The average duration between IVOId clinic visits was 6 days. There was a higher median daily IV Furosemide equivalent dose for inpatients compared to outpatients (80 mg vs. 40 mg respectively), which was due to longer days of IV diuresis in the inpatient group.

3.2. Acute diuretic administration outcomes

There was no significant difference between the daily net volume loss between inpatients and IVOId clinic groups (1159 ± 1044.7 vs. 944.4 ± 790.8 ml respectively, p = 0.46) with higher total weight loss (-9 ± 8.2 vs. -2.3 ± 2.1 lb respectively, p = 0.01), which was due to longer days of IV diuresis in the inpatient group (Table 2). There was a trend for more low blood pressure (SBP of <100 mmHg or DBP of <60 mmHg) episodes after IV diuretic administration in the inpatient group as compared to the IVOId group that did not reach statistical significance (SBP 4 vs. 0 episodes respectively, p = 0.14 and DBP 6 vs. 0 episodes respectively, p = 0.06). Both groups had similar rates of potassium (potassium level ≥ 5.1 mEq/L and ≤ 3.4 mEq/L) and renal abnormalities (≥25% for BUN and creatinine from baseline). Diuretics were increased by similar amounts from their baseline home dose after admission or IVOId diuresis (20 ± 24 vs. 40 ± 42.2 mg respectively, p = 0.35). No outpatients were admitted from the IVOId clinic for adverse events or need for further diuresis.

3.3. Longer-term outcomes

Inpatient and outpatient diuresis had similar 90-day outcomes, with the inpatients trending towards a higher number of cumulative readmissions that were not statistically different (Table 2). The outpatient group had post IV diuresis lab follow-up that was sooner than the inpatients (3.1 ± 2.2 vs. 28.1 ± 51.7, respectively; p = 0.04). Both groups had similar degrees of potassium and renal abnormalities on follow up labs. A Kaplan–Meier Curve (Fig. 2) shows a non-significant trend towards higher rates of readmissions for HF in the inpatient group by 90 days post discharge compared to admissions in the outpatient group (22.7% vs. 7.1% respectively; p = 0.37; Table 2). At 90 days after discharge there was 1 death recorded in the inpatient diuresis group and no deaths in the outpatient group (Fig. 3).

3.4. Costs

Inpatient stay for diuresis was associated with significantly higher total costs compared to outpatient diuresis ($9895.7 ± $8728.4 vs. $839.4 ± $370.6, respectively; p < 0.001).
patients in clinic setting have shown to have promise, [13–17] diuretic based decongestion strategies for volume overloaded HF management algorithms. Indeed, even though alternative outpatient IV patterns, lack of alternative options, or presence of institutional mandated, which may be partly due to established practice patterns that have clear decision trees for risk stratification as well as chronic obstructive lung disease exacerbations (goldcopd.org), which have clear decision trees for risk stratification as well as guidelines on therapies and treatment location (home, inpatient ward or intensive care unit). One major reason for these differences in guidelines is lack of high-quality data with which to make recommendations as the level of evidence for the ACC/AHA guidelines were mostly C (expert consensus) and some B (limited populations evaluated). In this report we evaluated a potential alternative to inpatient admission for ADHF - an IV diuresis clinic for lower-risk ADHF patients who would otherwise have been hospitalized.

We show that in a small group of ADHF patients who presented to the ED and were decongested as outpatients in the IVOiD clinic, the inpatient cohort were followed up significantly later than the outpatient cohort. IVOiD clinic group had lower total dose of IV diuretic administered and total weight loss with IV diuresis, which can be attributed to the longer length of stay observed in inpatient admissions compared to outpatient visits. This difference in discharge planning and post-hospitalization follow up, increase in adverse events as compared to patients with similar baseline characteristics who were hospitalized. IVOiD clinic group had lower total dose of IV diuretic administered and total weight loss with IV diuresis, which can be attributed to the longer length and total IV diuretic dose in the inpatient group. This difference in short term weight loss seen in the admitted patients was clinically compensated by doubling the IVOiD clinic’s group home diuretic dose until clinic follow up. Also, despite guideline recommendations on discharge planning and post-hospitalization follow up, the inpatient cohort were followed up significantly later than the IVOiD cohort.

Perhaps one of the major drivers for hospitalizing ADHF patients from the ED is the concern for adverse short and long-term outcomes. Index ADHF admissions have a 20% associated risk of 30-day rehospitalization and a nearly 30% 1-year mortality.[3,4,20] These statistics are driven by a subset of high risk patients[5–8] with high comorbidity burden or progression of disease. However, a significant portion ADHF patients in the ED are likely to be adequately treated in the outpatient setting. There are no studies providing an alternative decongestion strategy for other conditions like community acquired pneumonia [20] and chronic kidney disease [14–18]. These statistics are driven by a subset of high risk patients[5–8] with high comorbidity burden or progression of disease.
not at high risk for short-term morbidity and mortality [1, 8, 29–32, 21–28]. ADHF exacerbations are often caused by reversible factors, such as changes in diet or medications [33], and these account for 50% of all ADHF hospitalizations. In this report we excluded patients with high risk features [5–8] and evaluated for adverse outcomes with outpatient IV diuresis, including electrolyte abnormalities, renal failure, readmissions (30-day and 90-day for ADHF or all readmissions) and death. We found that in the studied cohort of patients there were no significant differences between any of the above parameters. There was a trend towards higher rates of readmissions for ADHF in the inpatient group versus the IVOiD group at 90 days, with 22.7% versus 7.1% respectively. There was low morbidity, renal failure, readmissions (30-day and 90-day for ADHF or all readmissions) and death. This was highly significant despite the small sample size. There were several limitations to this study. It had a small sample size which limited the ability to establish statistical significance on numerous results. Additionally, it was a single VA center study which further limited the number of patients studied and the applicability to other healthcare systems or populations. It was a non-randomized and non-blinded quality improvement project thus there may have been an inherent bias in patient selection or treatment.

Future larger multi-center randomized clinical trials are necessary to determine if outpatient IV diuresis can be a viable alternative to inpatient hospitalization for ADHF ED patients, with the potential promise of similar outcomes and saved costs.

5. Conclusions

An outpatient intravenous diuresis clinic may be a viable alternative for the diuresis in patients presenting with acute exacerbation of chronic heart failure to the currently accepted clinical practice of inpatient diuresis. Further studies are needed to validate this approach in a larger cohort and in multiple sites.

6. Contributorship

Ilia G. Halatchev, Wen-Chin Wu, Paul A. Heidenreich, and Jay R. McDonald were involved in the planning, data analysis and manuscript preparation. Sumitra Balasubramanian was involved in the data analysis and tables/figures generation. Elma Djukic and Kelly B. Ohlms were involved in the data gathering and tabulation.
Funding information/grant support

This was supported by Veterans Affairs St. Louis Heath Care System ePromise ProjectID 1,187,957 grant.

Ethical approval

The quality improvement (QI) project was approved by the VHA hospital’s QI/quality assurance (QA) board and research depart-
ment. The data storage, analysis and publication were approved by the Institutional Review Board (IRB) for an exemption (Saint Louis VA Medical System IRB reviewed and exempt this project e-pro-
mise#: 1215443).

Data sharing
Data may be obtained from a third party and are not publicly available. This material is the result of work supported with resources and the use of facilities at the St. Louis VA Health Care System and a St. Louis Health Care System Research Seed Grant Award from the US Department of Veterans Affairs.

Declaration of Competing Interest
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements
We would like to thank the Saint Louis VA Emergency Department for their care and patient assessment as well as the veterans who participated in the QI project.

References

[1] V.L. Roger, A.S. Go, D.M. Lloyd-Jones, E.J. Benjamin, J.D. Berry, W.B. Borden, D. M. Bravata, S. Dai, E.S. Ford, C.S. Fox, H.J. Fullerton, C. Gillespie, S.M. Hailpern, J. A. Heit, V.J. Howard, B.M. Kissela, S.J. Kittner, D.T. Lackland, J.H. Lichtman, L.D. Lisabeth, D.M. Mackm, G.K. Marcus, A. Marelli, D.B. Matchar, C.S. Moy, D. Mozaffarian, M.E. Mussolino, G. Nichol, N.P. Paynter, E.Z. Solomon, P.D. Sorlie, N. Sotoodehnia, T.N. Turi, S.S. Virani, N.D. Wong, D. Woo, M.B. Turner, Heart Disease and Stroke Statistics—2012 Update, Circulation, 125 (2012) 2–220. https://doi.org/10.1161/01.CIR.0000381323.0466.

[2] D. Lloyd-Jones, R.J. Adams, T.M. Brown, M. Carnethon, S. Dai, G. De Simone, T.B. Fuster, E. Geographic disparities in lifetime risk of cardiovascular disease: a national population-based estimation. Circulation, 2011 (2011) 134–143. https://doi.org/10.1161/CIRCULATIONAHA.110.988367.

[3] R.M. Mills, R.D. Kociol, W. Klaskala, B.G. Hammill, G.C. Fonarow, A.F. O’Connor, Effect of geographic disparities in access to care on survival in heart failure: the Framingham study, N. Engl. J. Med. 285 (1971) 1441–1446. https://doi.org/10.1056/NEJM19711223328503.

[4] W.B. Borden, D.M. Bravata, S. Dai, C. Gillespie, S.M. Hailpern, J.A. Heit, S.J. Kittner, D.T. Lackland, H. Judith, Heart disease and stroke statistics—2013 update: a report from the American heart association, Circulation. 127 (2013) 10–84. https://doi.org/10.1161/CIRC001318.82144.AA.Heart.

[5] C.W. Yancy, M. Jessup, B. Bozkurt, J. Butler, D.E. Casey, M.M. Colvin, M.H. Drazner, G.C. Fonarow, A.F. O’Connor, Heart failure with preserved ejection fraction: a comprehensive update on diagnosis, risk factors, and management, Circulation. 128 (2013) 2002–2010. https://doi.org/10.1161/CIRCULATIONAHA.113.010891.

[6] C.W. Yancy, M. Jessup, B. Bozkurt, J. Butler, D.E. Casey, M.M. Colvin, M.H. Drazner, G.C. Fonarow, A.F. O’Connor, Heart failure with preserved ejection fraction: a comprehensive update on diagnosis, risk factors, and management, Circulation. 128 (2013) 2002–2010. https://doi.org/10.1161/CIRCULATIONAHA.113.010891.
management of heart failure: A scientific statement from the American Heart Association, 2017. https://doi.org/10.1161/CIR.0000000000000490.

[30] B. Demissei, D. Postmus, J.G. Cleland, C.M. O'Connor, M. Metra, P. Ponikowski, J. Teerlink, G. Cotter, B.A. Davison, M. Givertz, D.M. Bloomfield, D. Veldhuisen, H. Dittrich, H.L. Hillege, A.A. Voors, Plasma biomarkers to predict or rule out early post-discharge events after hospitalization for acute heart failure, Eur. J Heart Fail. 19 (2017), https://doi.org/10.1002/ejhf.766.

[31] T. Ilva, J. Lassus, K. Siirilä-Waris, J. Melin, K. Pehkkurinen, K. Pulkki, M.S. Nieminen, H. Mustonen, P. Porela, V.P. Harjola, Clinical significance of cardiac troponins I and T in acute heart failure, Eur. J Heart Fail. 10 (2008) 772–779, https://doi.org/10.1016/j.ejheart.2008.06.009.

[32] K.S. Shah, A.S. Maisel, G.C. Fonarow, Troponin in Heart Failure, Heart Fail. Clin. 14 (2018) 57–64, https://doi.org/10.1016/j.hfc.2017.08.007.

[33] J.R. Kapoor, R. Kapoor, C. Ju, P.A. Heidenreich, Z.J. Eapen, A.F. Hernandez, J. Butler, C.W. Yancy, G.C. Fonarow, Precipitating Clinical Factors, Heart Failure Characterization, and Outcomes in Patients Hospitalized With Heart Failure With Reduced, Borderline, and Preserved Ejection Fraction, JACC Hear. Fail. 4 (2016) 464–472, https://doi.org/10.1016/j.jchf.2016.02.017.