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ORIGINAL ARTICLE

Prognostic role of diuretic failure in determining mortality for patients hospitalized with acute decompensated heart failure

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Abstract

Background Worsening heart failure (WHF) is defined as persistent or worsening symptoms of heart failure that require an escalation in intravenous therapy or initiation of mechanical and ventilatory support during hospitalization. We assessed a simplified version of WHF called diuretic failure (DF), defined as an escalation of loop diuretic dosing after 48 h, and assessed its effects on mortality and rehospitalizations at 60-days.

Methods We conducted a multicenter retrospective study between December 1, 2017 and January 1, 2020. We identified 1389 patients of which 6.4% experienced DF.

Results There was a significant relationship between DF and cumulative rates of 60-day mortality and 60-day rehospitalizations ($p=0.0002$ and $p=0.0214$). After multivariate adjustment, DF was associated with longer hospital stay ($p<0.0001$), increased rate of 60-day mortality ($p=0.026$), 60-day rehospitalizations ($p=0.036$), and a composite outcome of 60-day mortality and 60-day cardiac rehospitalizations ($p=0.018$).

Conclusions DF has a strong relationship with adverse heart failure outcomes suggesting it is a simple yet robust prognostic indicator which can be used in real time to identify high-risk patients during hospitalization and beyond.

Keywords Acute heart failure · Diuretic failure · Mortality · Worsening heart failure

Introduction

Between 2001 and 2014, there were 57.4 million hospitalizations for acute decompensated heart failure (ADHF) [1]. During hospitalization, patients with "persistent or worsening symptoms of heart failure requiring an escalation in intravenous therapy or initiation of mechanical and ventilatory support" are considered to have worsening heart failure (WHF) [2]. Since its conception, WHF has demonstrated a prognostic role in predicting mortality and rehospitalizations [3, 4], and has become an important clinical endpoint in randomized controlled trials [5–11]. However, there is a lack of standardization in its definition due to differences in the modality of rescue therapy used, the timing of WHF, and subjective assessment of symptoms present [12–14]. Currently, there are limited studies assessing the effects of increasing diuretic dose with or without the presence of WHF on heart failure outcomes. In this study, we introduce diuretic failure (DF), which is defined as an escalation in intravenous loop diuretic therapy after 48 h of stable dosing regardless of the presence of WHF. In doing so, we created a simplified prognostic marker in ADHF and assessed its effects on length of stay, mortality, and rehospitalizations.

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Materials and methods

Study population

This was a multicenter retrospective study at a single hospital system in Pennsylvania. We identified patients with an admission and discharge diagnosis of acute decompensated heart failure (ADHF), receiving intravenous diuretics between October 1, 2017 and January 1, 2020. Patients' baseline characteristics, medical history, medications, and laboratory values were obtained using the electronic medical record. There were 1641 patients who were eligible based on these screening criteria. The first encounter was used for patients with multiple admissions for heart failure. To eliminate confounding disease processes, 102 patients with shock, end-stage renal disease, cirrhosis, nephrotic syndrome, loculated pleural effusions, use of intravenous fluids upon admission, and vasopressor requirement were excluded. Of those 1539 patients, 150 were excluded for receiving less than 24 h of intravenous diuretics. This was to factor out patients who only received intravenous diuretics in the emergency department as well as ensure adequate therapy duration for comparison with the DF group. As a result, there were a total of 1389 patients assessed in this retrospective study.

Definitions

Initial hospital diuretic dose was the average daily intravenous diuretic dose for 48 h before escalation or de-escalation of dosing occurred. Specifically, DF was defined as an escalation of loop diuretic dosing after at least 48 h or the use of hemodialysis. Patients who had de-escalation of dosing followed by escalation were not considered to have DF. Transthoracic echocardiogram findings were reported if completed within 6 months of hospitalization. All echocardiogram findings were categorized into mild, mild to moderate, moderate, moderate to severe, and severe.

Statistical methods

Statistical analyses were conducted in R. Two-tailed p-values were used to assess statistical significance with values < 0.05 considered statistically significant. Mean and standard deviation were used for continuous variables and compared across DF and no DF groups with the Student's T test. Absolute frequencies were used for categorical variables and compared between groups using the chi-square test. Univariate analysis was conducted on all patient baseline statistics and medical history listed in Table 3 using logistic regression. Independent predictors of DF were identified by first stratifying predictors according to their p-value in the univariate analysis, using only those with p values below 0.5. Stepwise multivariate logistic regressions in both backward and forward directions were then used for feature selection and model generation. Association of DF with a length of stay, 60-day mortality, 60-day rehospitalizations, and composite outcome of 60-day mortality and cardiac rehospitalizations, were assessed using logistic regression with and without adjustment for covariates. Kaplan–Meier estimates were used to show the effects of DF on 60-day mortality and rehospitalizations, and compared using log-rank tests.

Results

Baseline characteristics

Between October 1, 2017 to January 1, 2020 there were 1389 individuals hospitalized for ADHF. Among which 6.4% (89) of the patients developed DF. Baseline characteristics for patients with and without DF are summarized in Table 1. Patients with DF were more likely to have peripheral edema, lower systolic blood pressure, lower initial hospital diuretic dose, higher BUN, and higher baseline creatinine ($p < 0.05$). They also were less likely to have an ICD or a history of hyperlipidemia ($p < 0.05$). The most common reasons for DF included persistent overload (33%), lack of urine output (33%), and failure of shortness of breath resolution (16%) (Table 2).

Rate of events in patients with diuretic failure

Cumulative rate of 60-day mortality for patients with and without DF was 19.1 and 7.08% respectively (HR 4.522, 97.5% CI 2.01 to 10.17; $p = 0.0002$) (Fig. 1). There was also a significant difference in rates of 60-day rehospitalizations; 39.32% of patients with DF were readmitted in comparison to 26.92% of patients without DF (HR 1.639, 97.5% CI 1.08 to 2.5; $p = 0.0214$) (Fig. 2).

Predictors of diuretic failure

Significant univariate predictors of DF included markers of renal function (potassium, BUN, creatinine), markers of right ventricular dysfunction (severity of pulmonary hypertension and lack of right ventricle contractility on echocardiogram), and markers of severity of heart failure (BNP and blood pressure) ($p < 0.05$) (Table 3). A multivariate model was created using gender, weight, troponin, hypertension, presence of an ICD, initial hospital diuretic dose, use of intravenous bumetanide, the severity of pulmonary hypertension and tricuspid regurgitation, and beta-blocker or mineralocorticoid antagonist use. Peripheral edema was found to be statistically significant between DF and non-DF group in

Table 1 Baseline characteristics of the study cohort divided into patients with and without diuretic failure

Variable	Absence or presence of DF		
	No DF ($n=1300$)	DF ($n=89$)	*P* value
Demographic data			
Age (years)	77 ± 12	77 ± 12	0.975
Males, n (%)	666 (51%)	53 (60%)	0.165
Weight (kg)	93 ± 29	95 ± 31	0.472
Risk factor			
Dyslipidemia	1077 (84%)	65 (73%)	0.028
Hypertension	1180 (91%)	75 (84%)	0.068
Diabetes mellitus	603 (46%)	44 (49%)	0.654
Chronic kidney disease	774 (60%)	52 (58%)	0.924
COPD	354 (27%)	22 (25%)	0.695
Peripheral vascular disease	168 (13%)	13 (15%)	0.769
CAD	709 (55%)	51 (57%)	0.691
Atrial fibrillation	642 (49%)	45 (51%)	0.916
Previous stroke	175 (13%)	8 (9%)	0.296
ICD placement	183 (14%)	5 (6%)	0.036
History of smoking	709 (55%)	46 (52%)	0.670
Objective data			
Systolic blood pressure (mm Hg)	140 ± 25	134 ± 23	0.012
Ejection fraction > 40%	848 (66%)	52 (60%)	0.315
Signs of HF			
Peripheral edema			< 0.001
0	296 (33%)	13 (21%)	
Trace	88 (10%)	2 (2%)	
1 +	171 (19%)	6 (10%)	
2 +	250 (28%)	32 (52%)	
3 +	72 (8%)	8 (13%)	
4 +	12 (1%)	1 (2%)	
Rales > 1/3	100 (9%)	12 (16%)	0.106
JVP > 10 cm	112 (18%)	4 (10%)	0.254
Laboratory data			
Serum sodium (mmol/L)	138 ± 4	138 ± 5	0.811
BUN (mg/dL)	27 ± 15	35 ± 19	< 0.001
Serum creatinine (mg/dL)	1.31 ± 0.61	1.54 ± 0.72	0.005
Brain natriuretic peptide (pg/dL)	861 ± 818	1044 ± 1029	0.105
Hospital medications			
Initial hospital diuretic dose (mg)	74 ± 67	60 ± 32	< 0.001

Data presented as mean and standard deviation for continuous variables and absolute frequencies for categorical variables

BUN blood urea nitrogen, *CAD* coronary artery disease, *COPD* chronic obstructive lung disease, *DF* diuretic failure, *HF* heart failure, *ICD* implantable cardioverter-defibrillator, *JVP* jugular venous pulse

baseline analysis (Fig. 3), but was not included in the multivariate analysis due to the lack of its documentation in the electronic medical records: 442 patients in the cohort did not have adequate documentation of peripheral edema severity. For the variable to fit in the model, there would have been a significant reduction in the sample size. In model performance, the training set had an accuracy of 0.6924, and a c-index of 0.8006. The predictive value of the model using these variables had an accuracy of 0.6667 and a c-index of 0.7012 in the holdout set.

Effects of diuretic failure on outcomes

Using logistic regression, patients with DF had a longer length of stay ($p < 0.0001$), increased rate of 60-day mortality ($p < 0.0001$), increased rate of 60-day

Table 2 Clinical characteristics resulting in DF

Reason for DF	(%)
Failure of SOB resolution	10 (11)
Increasing BNP	1 (1)
Lack of weight loss	5 (6)
Lack of urine output	29 (33)
Persistent overload	30 (34)
Not documented	14 (16)

BNP brain natriuretic peptide, *SOB* shortness of breath

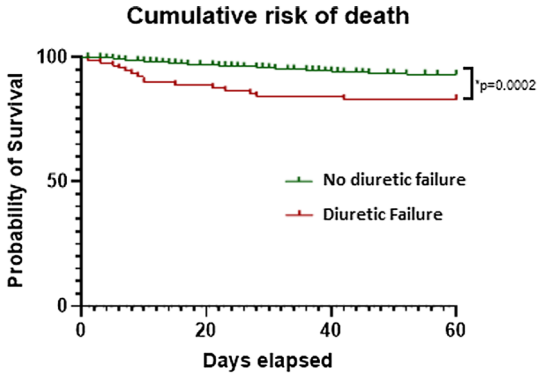

Fig. 1 Cumulative rate of mortality in patients with diuretic failure through 60-days

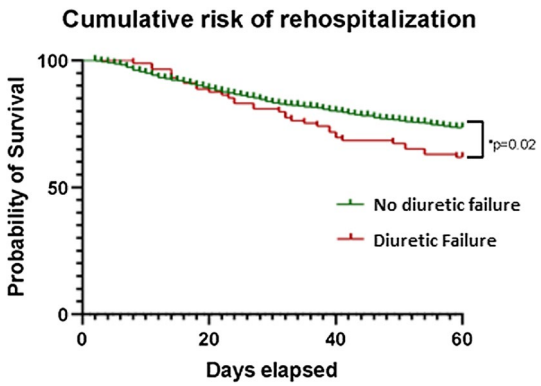

Fig. 2 Cumulative rate of rehospitalizations in patients with diuretic failure through 60-days

rehospitalizations ($p = 0.012$), and an increase in composite outcome of 60-day mortality and 60-day cardiac rehospitalizations ($p = 0.0004$) (Table 4). After adjustment for covariates associated with DF, DF remained an independent predictor of a longer hospital stay (OR 26.56, 97.5% CI 11.11 to 63.49; $p < 0.0001$), 60-day mortality (OR 2.07, 97.5% CI 1.06 to 3.84; $p = 0.026$), 60-day rehospitalizations (OR 1.63, 97.5% CI 1.03 to 2.57; $p = 0.036$), and a composite outcome of 60-day mortality and cardiac rehospitalizations (OR 1.78, 97.5% CI 1.09 to 2.84; $p = 0.018$).

Discussion

WHF has a prognostic role in predicting mortality and rehospitalizations in numerous post-hoc analyses [11–13]. However, there is a lack of standardization in its definition due to the reliance on subjective assessments of symptoms, a variety of therapies used, and different timing parameters. DF avoids these pitfalls by assessing the dosing of a single therapy, loop diuretics, after a set time of 48 h without requiring an assessment of heart failure symptoms. This marker is simple to use and generalizable to nearly all hospitalized patients with heart failure, as loop diuretics are a standard of care for decongestion [14]. Because of its ease of use, this could be applied in real-time during a hospitalization to identify patients who could benefit from more intensive monitoring and follow-up.

The primary finding of this study is that DF has a strong association with adverse heart failure outcomes including length of stay, 60-day mortality, 60-day rehospitalizations, and a composite outcome of 60-day mortality and cardiac rehospitalizations ($p < 0.05$). These findings are consistent with the broader literature on WHF [3, 4] and lack of diuretic response [15, 16] as a whole.

Notable univariate predictors of DF were markers of kidney dysfunction and right ventricular dysfunction: increasing BUN, creatinine, baseline potassium, pulmonary hypertension and tricuspid regurgitation, the severity of peripheral edema, decreasing eGFR, right ventricular contractility, and initial hospital diuretic dose. Patients with markers of right ventricular dysfunction are more likely to have venous congestion, renal dysfunction, and cardiorenal syndrome [17, 18]. As a result, they may require larger doses of diuretics due to renal dysfunction, increased neurohormonal response, and nephron remodeling [19]. Interestingly, the use of beta-blockers was an important component of the univariate and multivariate model, and was associated with an increased risk of DF. The negative inotropic effects from beta-blockers could potentiate the poor response to diuretics and cause DF [19].

We examined potential confounders of patient groups with disease severity, as indicated by a set of clinical variables. There was a statistically significant difference in the presence of peripheral edema of patients with and without DF ($p < 0.001$). 62% of patients without DF had 1 + peripheral edema or less compared to only 33% in the DF group. The driving force behind the significant difference is primarily the absence of peripheral edema in patients without DF. Jugular venous pulse, one of the most sensitive and specific markers for elevated right and

Table 3 Univariate and multivariate predictors of diuretic failure

Variable	Univariate model OR (97.5% CI)	*P* value	Multivariate model OR (97.5% CI)	*P* value
Demographic data				
Male gender	1.40 (0.91–2.18)	0.134	1.81 (1.00–3.34)	0.052
Weight (kg)	1.00 (1.00–1.01)	0.452	1.01 (1.00–1.02)	0.025
Objective data				
Systolic blood pressure (mm Hg)	0.99 (0.98–1.00)	0.017		
Peripheral edema	1.57 (1.23–1.99)	< 0.001		
Risk factor				
Dyslipidemia	0.56 (0.35–0.93)	0.021		
Hypertension	0.54 (0.31–1.03)	0.048	0.36 (0.17–0.82)	0.010
ICD placement	0.36 (0.13–0.82)	0.030	0.30 (0.07–0.89)	0.057
Laboratory data				
Serum sodium (mmol/L)	1.01 (0.96–1.06)	0.794		
Serum potassium (mmol/L)	1.52 (1.05–2.17)	0.023		
BUN (mg/dL)	1.03 (1.01–1.04)	< 0.001	1.03 (1.01–1.05)	< 0.001
Creatinine (mg/dL)	1.60 (1.19–2.09)	0.001		
Baseline troponin (ng/mL)	1.17 (1.00–1.45)	0.057	1.22 (1.01–1.67)	0.108
Brain-natriuretic peptide (pg/dL)	1.00 (1.00–1.00)	0.046		
eGFR (mL/min/1.73 m^2)	0.98 (0.97–0.99)	0.005		
Home medications				
ACE-I or ARB	0.71 (0.46–1.08)	0.112		
Beta-blocker	1.74 (0.91–3.78)	0.123	3.43 (1.33–11.78)	0.234
MRA	0.59 (0.28–1.29)	0.128	0.52 (0.18–1.23)	0.168
Home diuretic dose (mg)	1.01 (1.00–1.01)	0.022		
Echocardiographic data				
Ejection fraction	0.99 (0.98–1.00)	0.125		
Right ventricular contractility	1.26 (0.99–1.55)	0.042		
Aortic stenosis	0.98 (0.82–1.13)	0.761		
Aortic regurgitation	0.85 (0.65–1.08)	0.222		
Mitral stenosis	1.00 (0.69–1.33)	0.978		
Mitral regurgitation	0.85 (0.65–1.08)	0.222		
Tricuspid regurgitation	1.22 (1.04–1.42)	0.015	1.37 (1.10–1.69)	0.004
Pulmonary hypertension	1.22 (1.08–1.38)	0.002		
Hospital medications				
Initial hospital diuretic dose (mg)	0.99 (0.98–1.00)	0.015	0.99 (0.98–1.00)	0.007
Use of IV bumetanide (mg)	1.93 (0.78–4.11)	0.114	2.51 (0.90–6.22)	0.059

ACE–I angiotensin–converting enzyme–inhibitor, *ARB*, angiotensin receptor blocker, *BUN* blood urea nitrogen, *eGFR* estimated glomerular filtration rate, *ICD* implantable cardioverter–defibrillator, *IV* intravenous, *MRA* mineralocorticoid receptor antagonist, *OR* odds ratio

left-sided filling pressures, was not significantly different among the groups ($p = 0.254$) [20].

A notable limitation to our retrospective study is the limited sample size of patients experiencing DF: 89 of 1389 (6.4%). As mentioned above, the lack of integration of peripheral edema in the multivariate analysis due to the lack of documentation of it in the EHR is another limitation. Furthermore, this was a multicenter retrospective study in Pennsylvania, and its findings may not be generalizable to other populations. Additionally, DF only factored increases in loop diuretic dosing and not adjunct therapy like thiazide diuretics, mineralocorticoid antagonists.

In conclusion, DF is a simple yet potent prognostic marker for adverse heart failure outcomes including length of stay, mortality, rehospitalizations, and a composite outcome of mortality and cardiac rehospitalizations at 60-days. Markers of renal dysfunction as well as right ventricular dysfunction may help identify patients who may be at risk for DF. Given its association with poor

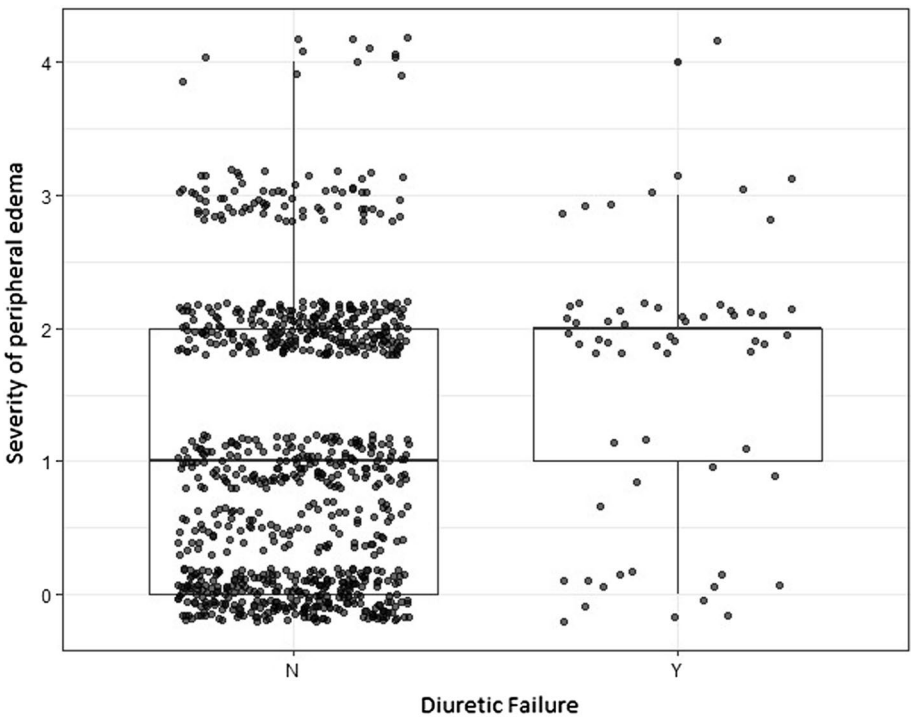

Fig. 3 Box plot comparing DF to the severity of peripheral edema across DF groups. Y corresponds to patients with DF and N corresponds to those who do not

Table 4 Association between diuretic failure and outcomes

Outcomes	Presence of DF			
	Unadjusted OR (97.5% CI)	*P* value	Adjusted[a] OR (97.5% CI)	*P* value
Length of stay	39.43 (16.52–94.11)	< 0.001	26.56 (11.11–63.49)	< 0.001
60-day mortality	3.10 (1.71–5.37)	< 0.001	2.07 (1.06–3.84)	0.026
60-day rehospitalizations	1.76 (1.12–2.73)	0.012	1.63 (1.03–2.57)	0.036
60-day mortality or cardiac rehospitalizations	2.26 (1.43–3.52)	< 0.001	1.78 (1.09–2.84)	0.018

[a]Adjusted for covariates found through stepwise multivariate logistic regression: gender, weight, hypertension, ICD placement, BUN, baseline troponin, beta blocker, MRA, tricuspid regurgitation, initial hospital diuretic dose, and use of intravenous bumetanide

CI confidence interval, *DF* diuretic failure, *OR* odds ratio

short-term outcomes, these patients should be identified and may benefit from earlier and more intensive follow-up.

Author contributions Conceptualization: SM, MPF, M S, AS, JM, AR, MNV; Methodology: SM, MPF, MS, AS; Formal analysis and investigation: MPF, MS, AS; Writing-original draft preparation: SM; Writing-review and editing: SM, MPF, MS, ASh, JM, AR, MNV; Resources: MNV; Supervision: MNV.

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Declarations

Conflict of interest The authors declare that there is no conflict of interest.

Ethical approval This research study was conducted retrospectively from data obtained for clinical purposes. We consulted extensively with the IRB of WellSpan York Hospital who determined that our study did not need ethical approval. An IRB official waiver of ethical approval was granted from the IRB of WellSpan York Hospital.

References

1. Akintoye E, Briasoulis A, Egbe A, Dunlay SM, Kushwaha S, Levine D, Afonso L, Mozaffarian D, Weinberger J (2017) National trends in admission and in-hospital mortality of patients with heart failure in the united states (2001–2014). J Am Heart Assoc 6(12):e006955
2. Tang WHW, Grodin JL (2015) Worsening heart failure: challenges as a therapeutic target. JACC Heart Fail 3:404–407
3. Cotter G, Metra M, Weatherley BD, Dittrich HC, Massie BM, Ponikowski P, Bloomfield DM, O'Connor CM (2010) Physician-determined worsening heart failure: a novel definition for early worsening heart failure in patients hospitalized for acute heart failure–association with signs and symptoms, hospitalization duration, and 60-day outcomes. Cardiology 115:29–36
4. Mentz RJ, Metra M, Cotter G, Milo O, McKendry C, Chiswell K, Davison BA, Cleland JG, Bloomfield DM, Dittrich HC, Fiuzat M, Ponikowski P, Givertz MM, Voors AA, Teerlink JR, O'Connor CM (2015) Early vs. late worsening heart failure during acute heart failure hospitalization: insights from the PROTECT trial. Eur J Heart Fail 17:697–706
5. Packer M, Colucci W, Fisher L, Massie BM, Teerlink JR, Young J, Padley RJ, Thakkar R, Delgado-Herrera L, Salon J, Garratt C, Huang B, Sarapohja T (2013) REVIVE heart failure study group. effect of levosimendan on the short-term clinical course of patients with acutely decompensated heart failure. JACC Heart Fail 1:103–111
6. Chen HH, Anstrom KJ, Givertz MM, Stevenson LW, Semigran MJ, Goldsmith SR, Bart BA, Bull DA, Stehlik J, LeWinter MM, Konstam MA, Huggins GS, Rouleau JL, O'Meara E, Tang WH, Starling RC, Butler J, Deswal A, Felker GM, O'Connor CM, Bonita RE, Margulies KB, Cappola TP, Ofili EO, Mann DL, Dávila-Román VG, McNulty SE, Borlaug BA, Velazquez EJ, Lee KL, Shah MR, Hernandez AF, Braunwald E, Redfield MM (2013) NHLBI heart failure clinical research network low-dose dopamine or low-dose nesiritide in acute heart failure with renal dysfunction: the rose acute heart failure randomized trial. JAMA 310:2533–43
7. Massie BM, O'Connor CM, Metra M, Ponikowski P, Teerlink JR, Cotter G, Weatherley BD, Cleland JG, Givertz MM, Voors A, DeLucca P, Mansoor GA, Salerno CM, Bloomfield DM, Dittrich HC, Investigators PROTECT, Committees, (2010) Rolofylline, an adenosine A1-receptor antagonist, in acute heart failure. N Engl J Med 363:1419–1428
8. McMurray JJ, Teerlink JR, Cotter G, Bourge RC, Cleland JG, Jondeau G, Krum H, Metra M, O'Connor CM, Parker JD, Torre-Amione G, van Veldhuisen DJ, Lewsey J, Frey A, Rainisio M, Kobrin I, Investigators VERITAS (2007) Effects of tezosentan on symptoms and clinical outcomes in patients with acute heart failure: the VERITAS randomized controlled trials. JAMA 298:2009–2019
9. Teerlink JR, Cotter G, Davison BA, Felker GM, Filippatos G, Greenberg BH, Ponikowski P, Unemori E, Voors AA, Adams KF Jr, Dorobantu MI, Grinfeld LR, Jondeau G, Marmor A, Masip J, Pang PS, Werdan K, Teichman SL, Trapani A, Bush CA, Saini R, Schumacher C, Severin TM, Metra M (2013) RELAXin in acute heart failure (RELAX-AHF) investigators serelaxin, recombinant human relaxin-2, for treatment of acute heart failure (RELAX-AHF): a randomised, placebo-controlled trial. Lancet 381:29–39
10. Felker GM, Lee KL, Bull DA, Redfield MM, Stevenson LW, Goldsmith SR, LeWinter MM, Deswal A, Rouleau JL, Ofili EO, Anstrom KJ, Hernandez AF, McNulty SE, Velazquez EJ, Kfoury AG, Chen HH, Givertz MM, Semigran MJ, Bart BA, Mascette AM, Braunwald E, O'Connor CM (2011) NHLBI heart failure clinical research network diuretic strategies in patients with acute decompensated heart failure. N Engl J Med 364:797–805
11. Weatherley BD, Milo-Cotter O, Felker GM, Uriel N, Kaluski E, Vered Z, O'Connor CM, Adams KF, Cotter G (2009) Early worsening heart failure in patients admitted with acute heart failure–a new outcome measure associated with long-term prognosis? Fundam Clin Pharmacol 23:633–639
12. Torre-Amione G, Milo-Cotter O, Kaluski E, Perchenet L, Kobrin I, Frey A, Rund MM, Weatherley BD, Cotter G (2009) Early worsening heart failure in patients admitted for acute heart failure: time course, hemodynamic predictors, and outcome. J Card Fail 15:639–644
13. Cotter G, Metra M, Davison BA, Senger S, Bourge RC, Cleland JG, Jondeau G, Krum H, O'Connor CM, Parker JD, Torre-Amione G, van Veldhuisen DJ, Milo O, Kobrin I, Rainisio M, McMurray JJ, Teerlink JR, Investigators VERITAS (2014) Worsening heart failure, a critical event during hospital admission for acute heart failure: results from the VERITAS study. Eur J Heart Fail 16:1362–1371
14. Čerlinskaitė K, Javanainen T, Cinotti R, Mebazaa A (2018) Global research on acute conditions team (GREAT) network acute heart failure management. Korean Circ J 48:463–480
15. Valente MA, Voors AA, Damman K, Van Veldhuisen DJ, Massie BM, O'Connor CM, Metra M, Ponikowski P, Teerlink JR, Cotter G, Davison B, Cleland JG, Givertz MM, Bloomfield DM, Fiuzat M, Dittrich HC, Hillege HL (2014) Diuretic response in acute heart failure: clinical characteristics and prognostic significance. Eur Heart J 35:1284–1293
16. Testani JM, Brisco MA, Turner JM, Spatz ES, Bellumkonda L, Parikh CR, Tang WH (2014) Loop diuretic efficiency: a metric of diuretic responsiveness with prognostic importance in acute decompensated heart failure. Circ Heart Fail 7:261–270
17. Testani JM, Khera AV, St John Sutton MG, Keane MG, Wiegers SE, Shannon RP, Kirkpatrick JN (2010) Effect of right ventricular function and venous congestion on cardiorenal interactions during the treatment of decompensated heart failure. Am J Cardiol 105:511–516
18. Tabucanon T, Tang WHW (2020) Right heart failure and cardiorenal syndrome. Cardiol Clin 38:185–202
19. Teerlink JR, Alburikan K, Metra M, Rodgers JE (2015) Acute decompensated heart failure update. Curr Cardiol Rev 11:53–62
20. Butman SM, Ewy GA, Standen JR, Kern KB, Hahn E (1993) Bedside cardiovascular examination in patients with severe chronic heart failure: importance of rest or inducible jugular venous distension. J Am Coll Cardiol 22(4):968–974