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Ambulatory intravenous treatment of decompensated heart failure: An effective, safe and cost-effective approach

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ABSTRACT

Introduction and objectives: The aim of this study was to evaluate the safety and efficacy of ambulatory intravenous (IV) treatment of decompensated heart failure (HF).
Methods: Retrospective analysis of all episodes of decompensated HF treated with IV diuretics at the HF day hospital from January 1 to December 31, 2016.
Results: A total of 192 episodes of HF decompensation were treated in 119 patients. Mean age and ejection fraction were 75 ± 11 years and 52 ± 15%, respectively, 65% were women and 63% had chronic kidney disease. All patients were on baseline oral furosemide (average dose 140 mg per day) and 21% on hydrochlorothiazide. The mean duration of each episode of ambulatory HF IV treatment was 3 ± 2 days and mean dose of treatment was 240 mg IV furosemide (80 mg/treatment day), 25 mg oral hydrochlorothiazide and 20 mEq oral potassium per treatment day. It was possible to avoid hospitalization in 81% of the episodes (n = 155 decompensations). This approach was associated with a decrease in direct hospital cost compared with hospitalization. The rate of complications was low: 4% (7 episodes) severe dyselectrolytemia and <1% (1 episode) symptomatic hypotension. There were no episodes of acute renal failure.

Abbreviations: eGFR: estimated glomerular filtration rate; HF: heart failure; IV: intravenous; LVEF: left ventricular ejection fraction; NT-proBNP: N-terminal pro-brain natriuretic peptide.

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Conclusions: A strategy of ambulatory IV diuretic treatment for HF decompensation could be effective and avoid hospital admission in a high number of patients, even in an elderly comorbid cohort with predominantly preserved LVEF. More importantly, this approach is safe with infrequent presence of dyselectrolytemia and symptomatic hypotension. This treatment was associated with a decrease in hospital cost.

Tratamiento diurético endovenoso ambulatorio en la insuficiencia cardiaca descompensada: una estrategia eficaz, segura y coste-efectiva

Palabras clave:
Insuficiencia cardiaca aguda
Tratamiento
Ambulatorio
Seguridad
Costes

RESUMEN

Introducción y objetivos: El objetivo fue evaluar la seguridad y la eficacia del tratamiento ambulatorio intravenoso (iv) de la insuficiencia cardiaca (IC) descompensada.
Métodos: Análisis retrospectivo de todas las IC descompensadas tratadas con diuréticos iv en el hospital de día de IC desde el 1 de enero al 31 de diciembre de 2016.
Resultados: Se trataron 192 episodios de IC descompensada en 119 pacientes. La media de edad fue de 75 ± 11 años y la fracción de eyección media, de 52 ± 15%; el 65% eran mujeres y el 63% tenían enfermedad renal crónica. Todos los pacientes recibían furosemida oral domiciliaria (dosis promedio: 140 mg/día) y el 21% hidroclorotiazida. La duración media de cada tratamiento iv ambulatorio fue 3 ± 2 días, y la dosis media por tratamiento de furosemida intravenosa fue de 240 mg (80 mg/día), de hidroclorotiazida 25 mg y de potasio oral 20 mEq. Fue posible evitar la hospitalización en 155 descompensaciones (81% de los episodios). Esta estrategia se asoció con una disminución en el coste hospitalario directo en comparación con la hospitalización. La tasa de complicaciones fue baja: 4% (7 episodios) diselectrolitemia grave y < 1% (un episodio) hipotensión sintomática. No hubo episodios de insuficiencia renal aguda.
Conclusiones: El tratamiento diurético ambulatorio iv en IC descompensada podría ser efectivo y evitar el ingreso hospitalario en un gran número de descompensaciones, incluso en una cohorte comórbida, añosa y con FEVI predominantemente conservada. Más importante aún, este enfoque es seguro y se asocia muy raramente con diselectrolitemia e hipotensión sintomática. Este tratamiento se asoció con una disminución en el coste hospitalario.

Introduction

Heart failure (HF) is a chronic disease that affects approximately 1–2% of the population[1] and its prevalence is increasing in recent years due to population aging and therapeutic advances[2]. The epidemiological dimension of HF, its clinical complexity, the impact on the quality of life of patients and the burden it represents for a health system with finite resources[3], make this syndrome one of the greatest health, organizational and economic challenges of the patients. HF natural history is characterized by episodes of frequent decompensation that often require hospitalization. Indeed, although overall HF hospitalization in the general population is 9%, it can be as high as 48% in patients with a previous HF hospitalization the preceding year[1,4]. Multidisciplinary comprehensive care programs for the disease have proven to be useful in reducing HF hospitalization[5]. One of the pillars of these programs is the empowerment of the patient to encourage self-care. They are based on the proper identification of signs and symptoms of decompensation, and on the consequent increase in oral diuretic treatment if necessary. The failure of this approach often entails a consultation at the emergency room and/or a hospital admission. However, complementary therapeutic strategies such as the administration of ambulatory IV diuretic treatment can allow clinical stabilization and, consequently, avoid hospitalization, with the benefits that this entails for both the patient and the health system. There is relatively scarce information regarding the use of this approach and the limited available evidence is based mostly on middle-aged patients with little comorbidity and reduced left ventricular ejection fraction (LVEF)[6–10]. Thus, the aim of this study was to evaluate the efficacy and security of ambulatory IV diuretic treatment for HF decompensation in a non-selected HF population followed up at the HF unit in a community hospital.

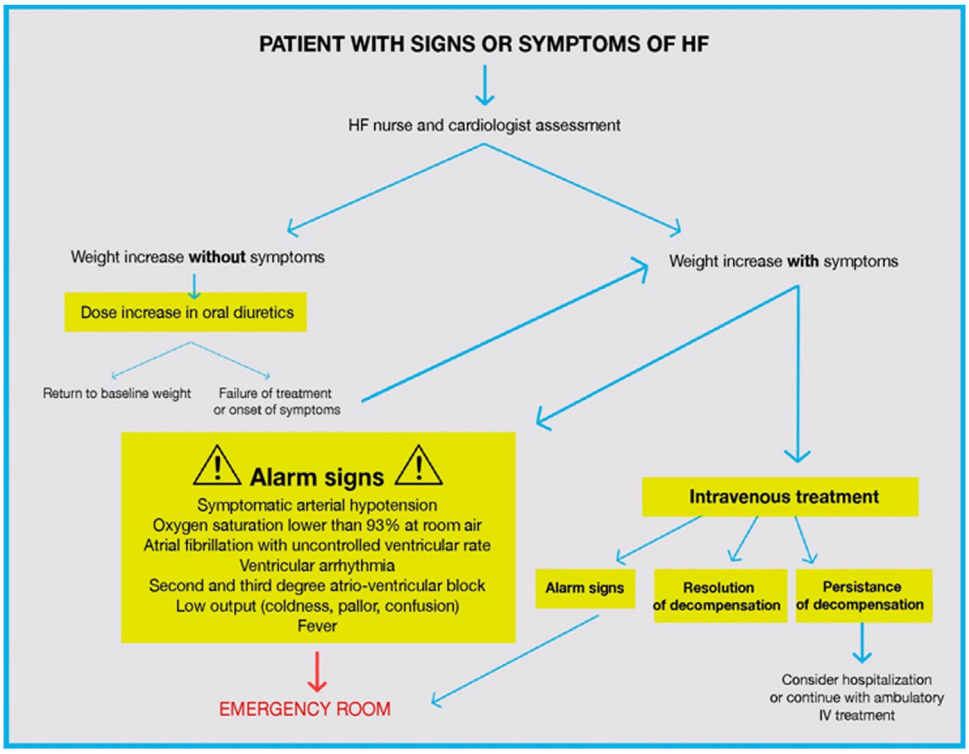

Fig. 1 – Treatment algorithm of decompensated heart failure patients at the heart failure day hospital. HF, heart failure; IV, Intravenous.

Methods

Single-center retrospective study carried out at the Hospital del Mar (Parc de Salut Mar) in Barcelona, Spain; a university hospital with 404 beds with no heart transplantation or ventricular assist device program. All consecutive episodes of HF decompensation treated with IV diuretics at the HF day hospital from 1 January to 31 December 2016 were included in the analysis. Medical charts were reviewed in order to obtain information on baseline characteristics and medications as well as treatment given in the acute episode. Patients were included in the analysis irrespective of their LVEF. The only exclusion criteria were the need of hospital admission due to the presence of alarm signs (Fig. 1) and patients on renal replacement therapy.

The day hospital operates working days from 8 am to 5pm and has 4 points of care with access to oxygen, possibility to perform blood tests and give IV medication. A trained HF nurse looks after the HF patients. Patients followed up at the HF Unit are advised to directly contact the day hospital whenever they feel more dyspneic, have edema or weight gain. The local cardiologist and case manager HF nurse can also refer patients for a same-day evaluation. Upon arrival, the patient is assessed by a local HF consultant. Diagnosis of decompensated HF is done based on signs and symptoms criteria established in clinical practice guidelines. Patients with alarm signs are referred to the emergency room to be held under close clinical observation. For the remainder of patients, treatment is given following an algorithm for HF decompensation (Fig. 1).

The standard treatment protocol lasts 3 consecutive days, without an overnight stay at the hospital. However, it can be shortened or expanded as per the treating physician's decision. Vital signs (blood pressure, heart rate and body weight) are measured daily. According to the protocol, IV furosemide is given at a dose of 20 mg every 30 min up to a total dose of 60 mg. Depending on the baseline per oral furosemide; IV furosemide treatment can be doubled (i.e. giving a total dose of 120 mg IV furosemide). Adjuvant treatment with 25 mg of oral hydrochlorothiazide and 25 mEq of oral potassium is also given to all patients. During the IV treatment, the baseline per oral diuretic is maintained. Blood test with renal function and electrolytes analysis is done on day 1 and 3 to guide treatment as necessary. Measurement of N-terminal pro-brain natriuretic peptide (NT-proBNP) is at discretion of the attending physician since it is not part of the mandatory protocol checklist.

The primary efficacy endpoint was the need of hospitalization at 30 days due to failure of ambulatory IV treatment. The primary safety endpoint was the presence of severe dyselectrolytemia that required IV treatment (serum potassium < 3 mmol/L), symptomatic hypotension or acute renal failure, defined as an absolute > 0.3 mg/dL or a relative $\geq 25\%$ increase in serum creatinine. HF with preserved LVEF was defined as a LVEF $\geq 50\%$ [11]. Anemia was defined as a hemoglobin < 13 g/dL in men and < 12 mg/dL in women. Chronic kidney disease was defined as an eGFR < 60 mL/min/1.73m^2.

The secondary endpoint was to analyze the cost associated with this approach. Since each patient has a personal

Table 1 – Baseline characteristics and usual treatment of the entire population and depending on the efficacy of ambulatory IV treatment.

Variables	All patients	Successful treatment	Failure of treatment	P
n	119	155	37	
Women	77 (65)	86 (55)	18 (49)	.469
Age, years	75 ± 11	75 ± 11	74 ± 12	.578
Ejection fraction, %	52 ± 15	50 ± 16	46 ± 16	.213
Preserved LVEF	67 (56)	88 (57)	18 (49)	.462
Atrial fibrillation	74 (62)	98 (63)	24 (65)	1.000
Coronary artery disease	33 (28)	40 (26)	11 (30)	.400
Moderate to severe valve heart disease	37 (31)	53 (34)	10 (27)	.443
COPD	44 (37)	46 (30)	15 (41)	.239
Anemia	69 (59)	86 (57)	19 (53)	.709
Chronic kidney disease	75 (63)	98 (64)	25 (68)	.848
Medication				
Beta-blocker	95 (80)	128 (83)	32 (86)	.806
ACE inhibitor/ARB	59 (50)	80 (52)	17 (46)	.586
MRA	37 (31)	42 (27)	15 (41)	.114
Oral furosemide dose, mg	140 ± 90	140 ± 90	140 ± 60	.862
Hydrochlorothiazide	21 (18)	31 (24)	12 (34)	.277
Oral potassium	17 (14)	28 (21)	10 (31)	.249

Data are expressed as (%) or mean ± standard deviation. COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; IV, intravenous; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist.

identification number that links all medical contact with the hospital, it was possible to calculate the direct cost of each episode of acute HF treated at the day hospital. This cost was compared with the mean cost of an emergency room visit lasting less than 12 h due to HF in 2016 and with the mean cost of a short hospitalization (3 days) due to HF in 2016. For this analysis, HF was defined with the code 428.xx according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM).

This investigation conforms to the principles outlined in the Declaration of Helsinki. Parc de Salut Mar Ethics Committee approved the research protocol (number 2017/7535/I).

Statistical analysis

Categorical variables are presented in absolute number and percentage and were analyzed with the Chi-square. Continuous variables are expressed as mean ± standard deviation or median and 25–75% percentiles. Between groups quantitative variables were analyzed using the Student's *t* test or Mann–Whitney *U* test according to the distribution of the data. The comparison of intra-group quantitative variables was performed with the Student's *t* test for paired data or the Wilcoxon test, as appropriate. Overall mortality among patients who were able to avoid hospitalization and patients who were finally admitted was compared with the log-rank test. Statistical analysis was performed with STATA version 22.0.0.0.0.

Results

During 2016, 192 episodes of HF decompensation were treated in 119 patients who attended the HF day hospital, which corresponds to approximately four decompensation episodes per week. The mean age of patients was 75 ± 11 years (44% ≥ 80 years, range 35–92) and the mean ejection fraction was 52 ± 15%. Baseline characteristics, comorbidities and medication before IV ambulatory treatment are described in Table 1. The study population had high basal diuretic need: all patients were on baseline oral furosemide, with an average dose of 140 mg per day and 21% were also under treatment with hydrochlorothiazide.

The mean duration of each episode of ambulatory HF IV treatment was 3 ± 2 days. In 18% of episodes, the decompensation was resolved with 1 day of ambulatory IV treatment, whilst 82% of decompensations required treatment for more than one day. There were no significant differences in baseline characteristics between these two groups of patients (Table 2). The mean dose of IV furosemide administered for each decompensation was 240 mg (80 mg/treatment day), that of hydrochlorothiazide 25 mg/treatment day and that of oral potassium 20 mEq/treatment day.

It was possible to avoid hospitalization in 81% of the episodes (*n* = 155 decompensations), while 19% (*n* = 37 decompensations) required hospital admission to complete the IV treatment. No significant differences in baseline characteristics between these 2 groups of patients were identified. However, 21% and 30% of descompensations that did not required an initial hospitalization needed a new ambulatory IV treatment due to new decompensation at 30- and 60-day follow-up, respectively. Regarding hospitalization after a first successful ambulatory IV treatment, it was needed in 17% and 20% of decompensations within at 30- and 60-day follow-up, respectively. Mortality rate was 4% at 30-day (40% due to HF), 14% at 6-month follow-up (53% due to HF) and 26% at 1 year (38% due to HF). During the average 28-month follow-up, 43% of patients died, with CV and HF mortality at 31% and 21% respectively. There was a trend (although not statistically significant) towards lower overall mortality

Table 2 – Baseline characteristics according to the need of more than 1- day IV ambulatory treatment to manage a single episode of decompensated HF.

Variables	1 day of treatment	More than 1 day of treatment	P
n	34	158	
Women	21 (62)	83 (53)	.349
Age, years	74 ± 13	74 ± 11	.979
Ejection fraction, %	50 ± 16	49 ± 16	.829
Preserved LVEF (>50%)	19 (56)	87 (55)	1.000
Atrial fibrillation	21 (62)	101 (64)	.846
Coronary artery disease	11 (33)	40 (26)	.390
Moderate to severe valve heart disease	12 (35)	51 (32)	.841
COPD	9 (26)	52 (33)	546
Anemia	20 (59)	85 (56)	849
Chronic kidney disease	21 (64)	102 (65)	.843
Medication			
Beta-blocker	29 (85)	131 (83)	1.000
ACE inhibitor/ARB	19 (56)	78 (49)	.572
MRA	8 (31)	49 (31)	.258
Mean oral furosemide dose, mg	150 ± 100	140 ± 80	.578
Hydrochlorothiazide	7 (25)	36 (26)	1.000
Oral potassium	9 (33)	29 (21)	.780

Data are expressed as (%) or mean ± standard deviation. Hb, hemoglobin; ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; COPD, chronic obstructive pulmonary disease; MRA, mineralocorticoid receptor antagonist.

at 30 and 60 days in patients who were able to avoid hospitalization compared to those who were finally admitted (30-day mortality, 4% vs 5.6%; 60-day mortality, 6% vs 11.1%; $P = .52$).

IV ambulatory treatment was safe and had a low rate of complications that required admission to the emergency department: 4% (7 episodes) due to dyselectrolytemia, < 1% (1 episode) due to symptomatic hypotension. There were no episodes of acute renal failure. Table 3 shows the changes in vital signs and blood parameters. Because not all patients had documented pre- and post- treatment values, only patients with both measures are included. There was a statistically significant decrease in weight (77 ± 15 vs 75 ± 15 Kg, $P < .001$) and NT-proBNP (3470 [1804–6869] vs 3154 pg/mL [1620–4992], $P = .013$), although NTproBNP was only measured in 21 episodes of decompensation. In addition, there was a statistically significant but clinically irrelevant decrease in renal function, potassium levels and blood pressure, which in no case required changes in the therapeutic plan.

The mean direct cost of an episode of acute HF treated at the day hospital (mean 3 ± 2 days) was 295.75€. A visit to the emergency room due to HF lasting less than 12 h had a mean cost of 276.38€ and a 3-day HF hospitalization had a mean cost of 1710.14€. Therefore, the use of the day hospital to treat a HF decompensation was associated with less cost compared to the traditional approach.

Discussion

The results of the present study show that a strategy of ambulatory IV diuretic treatment for patients with decompensated HF is effective and avoids a hospital admission in 81% of episodes treated, even in an elderly comorbid cohort with predominantly preserved LVEF. Despite the administration of diuretics at high doses, the presence of dyselectrolytemia (4%) and symptomatic hypotension (1%) was infrequent, which confirms that it is a safe procedure.

IV diuretic is the cornerstone of treatment of patients admitted due to decompensated HF without hemodynamic instability, and these patients only require control of diuresis, weight and blood analysis[11]. Therefore, and along with the economic pressure to reduce hospital admissions, outpatient alternative strategies have emerged in the management of patients with decompensated HF[12]. While these programmes have repeatedly and in various settings demonstrated a reduction in re-admissions for heart failure, there are reasonable doubts about their impact on medium-term global mortality[13]. Outpatient IV diuretic administration is one of the options available for the treatment of decompensated HF and our results are in the same direction as the evidence previously published in this same context[6–10]. Patients were on high baseline furosemide dose. Therefore, and in order to avoid the known breakdown phenomenon, our protocol considers the systematic co-administration of a thiazide diuretic. The daily IV furosemide dose was lower than in previous experiences. However, given the longer treatment cycles in our study (80% of patients receiving more than 2 outpatient clinic visits during index episode compared to 55% in previous studies), the mean final IV furosemide dose (250 mg) was consistent with previously published evidence[6]. Similarly to previous studies, a significant reduction in body weight and biomarkers (NT-proBNP) (when measured) was achieved, translating a clinically relevant diuretic response[6,7]. These studies also share a low percentage of optimal treatment with angiotensin-converting enzyme inhibitor, angiotensin receptor blocker and mineralocorticoid receptor antagonists, which in our case could be justified by the presence of chronic kidney disease and a lower prevalence of left ventricular dysfunction.

Table 3 – Changes in clinical and analytical parameters before and after IV ambulatory treatment.

Variables	*n*	Before IV treatment	After IV treatment	*P*
Creatinine, mg/dL	179	1.52 ± 1.18	1.60 ± 1.13	< .001
eGFR, mL/min/1.73 m^2	179	52 ± 26	48 ± 25	< .001
Sodium, mEq/L	177	138.1 ± 3.5	137.4 ± 4.0	.004
Potassium, mEq/L	176	4.3 ± 0.7	4.1 ± 0.6	.003
NT-proBNP, pg/mL	21	3470 [1804–6869]	3154 [1620–4992]	.013
SBP, mmHg	183	125 ± 25	122 ± 22	.003
DBP, mmHg	183	66 ± 12	63 ± 11	< .001
Heart rate, bpm	181	75 ± 15	74 ± 16	.508
Weight, kg	180	77 ± 15	75 ± 15	< .001

Data are expressed as *n* (%), mean ± standard deviation or median [interquartile range]. eGFR, estimated glomerular filtration rate; IV, intravenous; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Our series differs from those previously published in 2 relevant aspects that should be noted. First, with 192 HF decompensations treated it is the most extensive series published to date[6–10]. Second, the profile of patients is rather different to what has been published so far. Indeed, whereas in previous studies, age ranged from 55 to 71 years, our population was more than 5 years older (75 years) than what has been published to date and more than 40% of the patients were over 80 years. Moreover, the number of women almost doubled previous studies (15–40% vs 65% in our study)[6–10] and the prevalence of HF with preserved ejection fraction was markedly higher than in previous studies, probably in relation to the characteristics of a community heart failure unit. Finally, the presence of comorbidities was substantial. It is especially relevant the high presence of chronic kidney disease (63% of patients) because it might complicate the treatment with diuretics. However, we saw that although the treatment was associated with a small increase in serum creatinine, it did not reach the definition of acute renal failure nor motivate any change in treatment or required hospitalization. Interestingly, we could not identify any difference in baseline characteristics that allowed us to discriminate between patients in which treatment would be successful from those in which it would fail. Hence, our data suggests that it is reasonable to try the ambulatory IV approach in every patient given that the rate of complication was low. Overall, it is worth noting that the profile of patients treated in our day hospital resembles quite accurately patients with HF according to previous epidemiological studies carried out at a population level, with a mortality rate at 1-year, which is similar to patients with a recent HF hospitalization[1]. Interestingly, cause of death was not always due to HF or other cardiovascular mechanisms. Similarly to what has been published, worsening HF accounted for 21–53% of total mortality, depending on the time lapse from the decompensation[14]. Therefore, this study gives reassurance that ambulatory treatment with IV diuretics can be safely and effectively given to treat a broad spectrum of decompensated HF patients.

Previous studies have shown that hospitalization is the main cause of expenditure in HF patients[3]. Therefore, avoiding hospitalization has benefits not only for the patient, but also for the health system. There is evidence that ambulatory IV treatment is a cost-effective therapeutic approach[10,15] and, in our study, we also showed that ambulatory IV treatment is associated with a significant decrease in healthcare direct costs.

Limitations

Our data must be interpreted with caution since this is a single center and retrospective report and thus some data could not be captured. In addition, the size of our sample is relatively small. Changes in NTproBNP during treatment, despite being a robust marker of effective decongestion, was only recorded in 21 decompensations, since it was not a mandatory parameter but at the discretion of the treating clinician. However, it is noteworthy that even in such a small sample the differences were statistically significant. Finally, the treatment protocol could be adjusted as per the attending cardiologist criteria. Although this makes it very difficult to guarantee a complete standardization of treatment, such variability reflects the usual clinical practice that can be seen at different levels such as the emergency room or the hospitalization ward.

Conclusions

A strategy of ambulatory IV diuretic treatment for patients with decompensated HF could be effective and avoid a hospital admission in 81% of episodes, even in an elderly comorbid cohort with predominantly preserved LVEF and chronic kidney disease. Despite the administration of diuretics at high doses, the presence of dyselectrolytemia (4%) and symptomatic hypotension (1%) was infrequent, thus confirming that it is a safe procedure. Moreover, this treatment was associated with a decrease in hospital cost. However, this approach should be validated in prospective randomized controlled trials.

Conflicts of interest

The authors have nothing to declare.

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What is known about the subject?

- HF is a global pandemic and its prevalence is increasing.
- HF health expenditures are considerable, mainly because patients with HF experience high rates of hospitalizations.
- The ambulatory IV diuretic treatment in decompensated HF could avoid hospitalization, with benefits for both the patient and the health system.
- There is relatively scarce information regarding the use of ambulatory IV diuretic treatment in HF.

Does it contribute anything new?

- The ambulatory IV diuretic treatment in decompensated HF is effective and avoids hospital admissions, even in an elderly comorbid cohort with predominantly preserved LVEF.
- This strategy is safe despite the administration of diuretics at high doses.
- This treatment is associated with a decrease in hospital cost.

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