

Ambulatory management of acute decompensation in heart failure

ABSTRACT

Heart failure is an increasingly prevalent chronic condition which causes substantial morbidity and mortality, placing an increasing economic burden on health care. Hospitalizations as a result of heart failure are projected to increase considerably over the next two decades. A robust restructuring of existing heart failure treatment models in the UK is needed to enable an integrated seamless transition of care across the community, primary care and hospital networks. This has to be achieved with the patient as a partner in health care as a part of a multidisciplinary approach. This uses innovative strategies such as ambulatory treatment (including intravenous diuretics, remote and telemonitoring) as well as shifting heart failure treatment to the community and to patients' homes. This article analyses the existing evidence for ambulatory management of acute decompensated heart failure and looks at future strategies for restructuring care.

Around 900 000 people in the UK suffer from heart failure (National Institute for Cardiovascular Outcomes Research, 2017). Heart failure was the primary diagnosis for 66 695 admissions and the secondary diagnosis in 20% more admissions in England and Wales in 2015–16 (National Institute for Cardiovascular Outcomes Research, 2017). Compared to data from 2014–15, there was a 17% increase in the number of admissions for heart failure (56 915) in 2015–16. Heart failure also directly causes or complicates about 5% of all emergency hospital admissions, consumes

about 2% of the total NHS expenditure and leads to 10% of bed occupancy (National Institute for Health and Care Excellence, 2018), and re-admission rates for patients with heart failure are high (20–25% within 1 month and 40% within 6 months). Admission as a result of heart failure portends considerable mortality during an inpatient stay (8.9%), extending to 26.7% at 1 year for those who survive to discharge (National Institute for Cardiovascular Outcomes Research, 2017). Admissions for heart failure are predicted to double in the next 25 years as a result of the ageing population and better survival from myocardial infarction (National Institute for Health and Care Excellence, 2018). These factors, coupled with the associated comorbidity, are likely to place a substantial economic burden on health-care resources in the UK.

Patients with chronic heart failure usually have a long period of stable symptoms with breathlessness, peripheral oedema and fatigue. Gradual deterioration generally occurs over the weeks preceding hospital admission. If this deterioration could be detected and managed early before presenting as acute decompensated heart failure, hospital admissions could potentially be avoided.

In the National Heart Failure Audit, around half of all patients admitted with heart failure had moderate to severe peripheral oedema which was associated with a longer stay in hospital (National Institute for Cardiovascular Outcomes Research, 2017). It has been proposed that improved detection and management of oedema in the community could reduce the length of in-hospital stay and even prevent admission (National Institute for Cardiovascular Outcomes Research, 2017). This is usually attempted by increasing the dose of oral loop diuretics such as furosemide or bumetanide followed by the addition of thiazide (or thiazide-like) diuretics such as bendroflumethiazide or metolazone. If these strategies fail, hospitalization is usually deemed necessary for intravenous diuretic administration. Intravenous diuretics are usually administered continuously (every 24 hours) until adequate decongestion (measured by negative fluid balance, weight loss and improvement in symptoms) is achieved.

Bolus administration of intravenous diuretics is as efficacious and safe as continuous administration (Felker et al, 2011). In the absence of pulmonary oedema, cardiogenic shock, uncontrolled arrhythmia or ongoing myocardial ischaemia, most hospitalized patients with heart failure do not usually require invasive investigations or therapeutic interventions other than intravenous diuretics for decongestion. The monitoring that is usually performed during hospitalization such as recording blood pressure, heart rate, oxygen saturation and weight, and

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investigations such as echocardiography, electrolyte and N-terminal pro B-type natriuretic peptide (NT-proBNP) measurements, can be performed in the outpatient setting.

Most admissions for heart failure (80%) are via the emergency department, but Collins et al (2013) estimated that at least 50% of these patients could be safely discharged. The deterioration leading to acute decompensated heart failure which triggers the need for hospitalization is a crucial milestone in the time course of a patient with heart failure as hospital admission, the length of hospital stay and the number of hospitalizations all predict poor quality of life and are also independently associated with higher mortality (Solomon et al, 2007). There is no clear evidence that hospitalization on its own improves outcomes. This is relevant as in the first 2–3 months following discharge, up to a third of patients with heart failure experience adverse events such as re-hospitalization or death (Gheorghiadu et al, 2006).

Recurrent hospitalization is a burden to patients with heart failure and uses scarce health-care resources, so strategies have been trialled to circumvent the need for hospital treatment. These include ambulatory intravenous diuretic administration, multidisciplinary care to treat the comorbidities that can contribute to acute decompensated heart failure and improved transitional care. This article reviews the evidence for these approaches and the potential for wider and more uniform implementation in the UK.

Ambulatory intravenous diuretic programmes

Table 1 (available at www.bjhm.co.uk) summarizes the various outcome measures used in the published ambulatory treatment strategies for acute decompensated heart failure. In one of the earliest published studies that evaluated outpatient intravenous diuretics for acute decompensated heart failure, Ryder et al (2008) retrospectively examined outcomes of 107 patients as a part of the hospital-based disease management programme. Patients with significant weight gain (2 kg over 2 days) refractory to increases in oral dose of diuretics as advised by a heart failure specialist nurse were assessed by a physician and treated with intravenous furosemide. Patients with paroxysmal nocturnal dyspnoea, right heart failure or other features suggesting instability were given intravenous diuretics as first line. Relatively smaller doses of intravenous furosemide (40–80 mg) were used compared to subsequent studies (detailed below). The majority of patients (72%) responded well to this strategy, resulting in significant weight loss, improvements in New York Heart Association (NYHA) class and reductions in NT-proBNP levels. This ambulatory strategy prevented approximately 30% of heart failure admissions, but 28% did not avoid hospitalization. Predictors of non-response to ambulatory treatment strategy included systemic hypotension, prior increase of oral diuretic dose and concurrent beta-blocker usage or uptitration of beta-blockers. Renal failure contributed to hospitalization in one patient and there were two deaths among patients who required hospitalization.

Hebert et al (2011) enrolled 577 patients with heart failure and left ventricular ejection fraction $\leq 40\%$ by

echocardiography in a heart failure disease management programme. All patients were educated to use a sliding scale of oral furosemide together with heart failure education and titration of medication. A weight gain of ≥ 5 lb despite the sliding scale (reflecting refractoriness to oral diuretic) triggered eligibility to use the ambulatory open access intravenous diuretic service (managed by a physician or nurse practitioner). Over 20% of patients ($n=130$) used the service. A single bolus dose of intravenous furosemide was used with an option to add a subsequent infusion (10–20 mg/hour for 6–8 hours) and 5 mg oral metolazone. Patients were given 40 mEq of oral potassium per 1000 ml of urine output. The highest number of visits required was 14. Use of the ambulatory intravenous diuretic service was much higher among NYHA class IV patients and hospitalized patients. There was no documented adverse event (change in creatinine level or hypokalaemia) and no difference in mortality compared to patients who did not use the service.

Lazkani and Ota (2012) presented a case series of seven patients (four with heart failure with reduced ejection fraction and three with heart failure with preserved ejection fraction) who presented with recurrent symptoms of decompensated heart failure within 30 days of discharge. During the study, a transitionalist physician (an acute physician who also works in outpatient and community settings to foster integration between primary and secondary care) reviewed patients before and after discharge and outlined a post-discharge care plan including education and instructions to uptitrate oral diuretics for 24 hours if patients experienced weight gain (≥ 3 lb), increased breathlessness and oedema. If adequate improvement was not noted, patients were reviewed by the physician. Patients whose breathlessness resolved were discharged and those who remained breathless were given intravenous diuretic the next day. If symptoms worsened, patients were transferred to the emergency department or admitted. Intravenous diuretic was given with oral metolazone and the dose of intravenous diuretic was determined by the physician in the same way as any standard encounter. Oral potassium supplement was given to all patients (dose based on the dose of intravenous diuretic). Six patients were discharged after one stay (maximum 12 hours) and one patient needed an extra stay. None of the patients was admitted for heart failure in the next 30 days.

Schipper et al (2012) developed a service whereby a dedicated heart failure nurse practitioner worked with staff nurses in a pre-existing non-specialized infusion centre (also used for other conditions), with concurrent delivery of ambulatory intravenous loop diuretic therapy along with self-care education for those patients with heart failure deemed to be at high risk of re-hospitalization. This study reported the outcomes of 23 patients who were treated in the service. The median dose of intravenous furosemide administered was 120 mg. There were isolated reports of mild transient hypokalaemia without accompanying clinically significant arrhythmia, and 14 patients required hospitalization despite the ambulatory service. Three patients were completely free of admissions for >180 days.

Makadia et al (2015) compared the outcome of 106 consecutive patients treated with intravenous diuretics following evaluation by a cardiologist in the John Hopkins Bayview Diuresis Clinic with outcomes in 143 patients who were hospitalized for intravenous diuretics (over a 15-month period). Heart failure education, outpatient care and assessment of social needs were part of the service. Mean age was similar in both groups (68.2±13 years in the clinic group *vs* 69±16 years in the hospitalized group). Study outcomes included urine output, hospitalizations and cost savings. The overall mean intravenous furosemide dose was 100 mg and treatment led to considerable diuresis (average urine output 1460±730 ml), weight loss of 2.3±1.8 kg, three fewer days in the hospital per 180 days per patient and an estimated annual saving of \$12 113 per patient.

Buckley et al (2016a) studied 60 consecutive patients with chronic heart failure who had symptoms and signs of congestion (irrespective of ejection fraction), who received intravenous furosemide on an ambulatory basis. They used a standardized protocol with an initial bolus injection followed by a 3-hour infusion of furosemide (20 mg/hour) in patients with early signs of decompensation in the community. Direct patient care was provided by a specialist nurse practitioner with help from a dedicated nurse and a clinical pharmacist who assessed medication adherence, and performed medication reconciliation and optimization. There was input from physicians, a diabetes specialist, nutritionist and palliative care specialist as required. Patients using the intravenous service were stable with systolic blood pressure >90 mmHg and signs of early decompensation.

The diuretic dosing regimen chosen was based upon the patient's usual oral diuretic dose and strategies included: low dose (20 mg bolus), standard dose (20 mg bolus), high (200 mg bolus followed by 20 mg/hour infusion with provision for further 200 mg bolus if inadequate urine output) and mega dosage regimen (200 mg bolus followed by 20 mg/hour infusion with provision for further 200 mg bolus as well as thiazide diuretic if inadequate urine output) as appropriate. Efficacy outcomes included urine output and weight loss. Safety outcomes were hypokalaemia, worsening of renal function and ototoxicity. Patients were followed up in a separate clinic or by telephone at 30 days. This study consisted of an 'advanced heart failure population' since before treatment, more than 75% of patients had NYHA class III or IV symptoms and nearly 50% of patients were on high oral doses of furosemide (>300 mg/day), suggesting that a large proportion was resistant to oral diuretics. Of patients 55% required only one visit. The median dose of diuretic used was 240 mg oral furosemide or equivalent. There was considerable weight loss and increased urine output across all groups of patients and across differing dosing regimens. Adverse events included mild renal impairment (8.9%), mild (2.7%) and severe hypokalaemia (0.9%) with full recovery; there was no arrhythmia or ototoxicity. Heart failure hospitalization rates were 9.4% at both 30 and 60 days and there were no deaths. This study showed that ambulatory administration of high dose intravenous furosemide is a safe and efficacious

alternative to hospitalization for the management of acute decompensated heart failure. This strategy also halved health-care costs compared to a hospitalization-based strategy for acute decompensated heart failure (Buckley et al, 2016b).

Ambulatory intravenous diuretic experience in the UK

There is a relative paucity of published UK data regarding ambulatory treatment of acute decompensated heart failure. Early data from the University Hospital of North Staffordshire ambulatory heart failure unit (Aston et al, 2011) showed a notable reduction in hospital bed-days occupied by patients with heart failure and considerable cost savings.

The British Heart Foundation funded a pilot project in which 10 NHS organizations implemented community intravenous diuretic services over a 2-year period (Brightpurpose, 2014). In this, 96 patients received a total of 126 intravenous diuretic interventions (average length of treatment 7 days). Patients received either once or twice daily bolus doses (usually titrated, ranging from 40–250 mg). The community intravenous diuretic strategy was efficacious (79% avoided hospital admission, 63% achieved target reduction in oedema and weight loss) and cost-effective (869 bed days saved and £199 458 net savings over the pilot duration). It also improved patient experience: 100% of patients and 93% of carers expressed a preference for community-based treatment, and 100% of patients and 96% of carers said they would choose such strategies again in the future.

Banerjee et al (2012) described results from a 1-year pilot study, during which 17 patients were treated with intravenous furosemide (daily double bolus or as single treatment in the form of a bolus and/or infusion of intravenous furosemide for three consecutive days) on an ambulatory basis over 3 days. This small study showed that ambulatory intravenous diuretic administration can also be effective (through improvement in breathlessness, reduction in weight), safe (without leading to major derangements in renal function, electrolyte imbalance or drops in blood pressure) and lead to potential cost savings (by preventing hospital admissions).

Preliminary data from the authors' ambulatory heart failure unit at Aintree University Hospital show that a specialist nurse-delivered heart failure disease management programme, including access to intravenous diuretics and multidisciplinary care, can provide safe, cost-effective treatment in complex patients with heart failure with considerable comorbidities including cardiorenal syndrome. This reduced the need for hospital admissions and length of stay (Nyjo et al, 2017; Rawat et al, 2017).

Transitional care services for heart failure

Over two decades ago, the landmark study by Rich et al (1995) showed that nurse-directed, multidisciplinary intervention improved quality of life, reduced hospitalizations and was cost effective. Subsequently, a range of transitional care heart failure interventions have been incorporated as a part of post-discharge heart failure management including heart failure education, promotion of self-care and medication adherence,

Table 2. Treatment and outcome

Characteristic	Banerjee et al (2012)	Buckley et al (2016a)	Hebert et al (2011)	Ryder et al (2008)	Schipper et al (2012)	
Daily furosemide dose	80–100 mg	240 mg (range 80–800 mg)	40 mg mostly, up to 200 mg	40–80 mg	240 mg	
Primary outcome	Weight loss	0.5–5 kg (88% patients)	Median 1.1 kg (range 0.6–1.3 kg)	–	2 kg	1 kg (mean)
	Urine output	NA	Median 1.1 litres (range 0.6–1.4 litres)	–	–	1.4 litres (mean)
	Improvement in dyspnoea	94% patients	NA	NA	Improved NYHA class ($P < 0.001$)	NA
Adverse event (%) [*]	Renal impairment	NA	8.9	0	0.93	–
	Mild hypokalaemia	NA	2.7	0	0	–
	Severe hypokalaemia	NA	0.9	0	0	0
Heart failure admission rate (%)	30-day	17.6	18.3	–	18	–
	60-day		21.7	–	–	–
	Death		0	0	1.9	–

^{*} There were no episodes of hypotension, ototoxicity or mortality. NA = not available; NYHA = New York Heart Association.

changes in lifestyle and a uniform mechanism to contact health-care personnel (e.g. patient hotlines). A meta-analysis of 53 randomized controlled trials including 12 356 patients by Van Spall et al (2017) analysed the efficacy of heart failure transitional care services on decreasing all-cause death and readmissions following hospitalization for heart failure. When transitional interventions were compared to standard of care, nurse home visits were the most efficacious and cost efficient in significantly reducing all-cause mortality (ranking P -score 0.6794, relative risk 0.78, 95% confidence interval 0.62–0.98) and readmissions (ranking P -score 0.8365, incident rate ratio 0.65, 95% confidence interval 0.49–0.86). Disease management clinics (incorporating follow-up visits at a hospital or community-based clinic, with comprehensive and multidisciplinary heart failure management) also significantly reduced all-cause mortality (ranking P -score 0.6368, relative risk 0.80, 95% confidence interval 0.67–0.97) and readmissions (ranking P -score 0.5691, incident rate ratio 0.80, 95% confidence interval 0.66–0.97). Nurse care management (nurse home visits combined with telephone support) significantly reduced all-cause readmissions (ranking P -score 0.6168, incident rate ratio 0.77, 95% confidence interval 0.63–0.95). However, telemonitoring, telephone follow up, pharmacist and educational interventions did not significantly alter outcomes. The findings were largely similar to those of two previous reviews of transitional care (Takeda et al, 2012; Feltner et al, 2014).

Discussion

Based on this evidence (small non-randomized studies), an ambulatory intravenous diuretic administration strategy in heart failure specialist units incorporating a multidisciplinary approach and robust transitional care is a

safe, efficacious, cost-effective approach to managing acute decompensated heart failure in patients with numerous comorbidities, irrespective of the ejection fraction.

There is considerable heterogeneity in the ambulatory intravenous diuresis and transitional care approaches that have been trialled. Inclusion and exclusion criteria were similar with some exceptions (Tables 2 and 3). Weight loss and urine output were the most commonly measured primary outcomes while renal function, electrolyte disturbance and hypotension were the most commonly monitored safety outcomes. There was no unifying dosing regimen. Average doses of furosemide ranged from 40 mg to 460 mg and some studies had standardized protocols. Some centres used specialist nurses to deliver ambulatory intravenous diuresis (Schipper et al, 2012; Buckley et al, 2016a), while in others a physician delivered the service with specialist nurse support.

A third to half of re-admissions in patients with heart failure are the result of non-cardiac causes as most patients with heart failure (particularly those with heart failure with preserved ejection fraction) have comorbidities which contribute to a substantial proportion of admissions (Ponikowski et al, 2016). A multidisciplinary approach in an ambulatory heart failure management unit using advice from other specialities is crucial to improving the management of comorbid conditions. For instance, patients with advanced chronic kidney disease were excluded from some studies (Makadia et al, 2015; Buckley et al, 2016a), but these patients often require and benefit from higher doses of loop diuretics (Oh and Han, 2015). The authors believe that patients with advanced chronic kidney disease and acute decompensated heart failure can be treated in an ambulatory heart failure unit with access to intravenous diuretics, although this requires close liaison with the renal team.

Table 3. Inclusion and exclusion criteria for ambulatory intravenous diuretic treatment

Inclusion criteria	Diagnosis of heart failure (systolic or diastolic)
	Signs and symptoms of congestion (dyspnoea, paroxysmal nocturnal dyspnoea, oedema)
	Weight gain (resistance to oral diuretic uptitration)
	Haemodynamic stability – clinician's perception, systolic blood pressure >90 mmHg
Exclusion criteria	Concern of acute medical or cardiovascular disease precipitating heart failure (e.g. new arrhythmia, acute coronary syndrome, pulmonary embolism)
	Need for emergent medical treatment
	Perceived high clinical risk as outpatient (based on clinical parameters or blood tests)
	Old age or frailty precluding ambulatory treatment
	Advanced or end-stage chronic kidney disease
	Need for supplemental oxygen

An ambulatory approach also allows patients with acute decompensated heart failure to receive hospital-based treatment without needing hospitalization. This could lead to a feeling of increased control in managing their condition, reinforcing the idea of the patient being a 'partner in health care'. An open access ambulatory heart failure treatment centre also avoids delays in presentation via traditional routes such as emergency departments, which are usually busy and where the first point of medical contact for these patients is usually with junior doctors who are relatively inexperienced in managing acute decompensated heart failure. An ambulatory heart failure treatment model can ensure better streamlining of standard heart failure care and provision of early follow up after treatment.

Adverse consequences of patients with heart failure being hospitalized include the risk of hospital-acquired infections, reduced mobility and consequent pressure ulcers, loss of confidence and depression. Most studies lack patient-reported outcome measures or patient satisfaction questionnaires pertaining to ambulatory heart failure management strategies, with certain exceptions (Brightpurpose, 2014). Larger studies with longer follow up are needed to assess if there is an effect on areas such as mortality and patient-reported outcomes.

Transitional care such as nurse home visits, nurse care management and disease management clinics is efficacious and cost effective in reducing all-cause mortality and readmissions (Van Spall et al, 2017). However, while the European Society of Cardiology guidelines advocate patient self-care education and early physician follow up, they do not specifically recommend individual transitional services (Ponikowski et al, 2016; Van Spall et al, 2017). As nearly half of readmissions can be attributed to deficiencies in transitional care (Phelan et al, 2009), combining transitional care services with ambulatory heart failure management will be important in improving heart failure outcomes.

It is also important that the ambulatory approach of treatment is extended to all suitable patients with heart failure (who fulfil inclusion criteria), irrespective of ejection fraction. This will help to develop a standardized model in terms of staffing involved, dosing regimens and robust integration of ambulatory care with transitional care.

Future directions and relevance to the UK

Several new technologies have been analysed to remotely monitor patients in order to help reduce adverse outcome. The CHAMPION multi-centre randomized control trial evaluated the effects of a wireless device implanted in the pulmonary artery using a minimally invasive procedure which continuously measures and transmits data on pulmonary artery pressure. Using this data to adjust heart failure medications to keep the pulmonary artery diastolic pressure 8–20 mmHg led to a 37% reduction in hospitalizations for heart failure (hazard ratio 0.63, 95% confidence interval 0.52–0.77, $P < 0.0001$) (Adamson et al, 2011).

Implantable devices such as cardiac resynchronization therapy pacemakers and internal cardioverter defibrillators enable continuous remote monitoring of arrhythmic burden, intrathoracic impedance changes to help assess congestion and changes in autonomic function. Remote recognition of these predictors of decompensation helps to time early intervention and thereby prevent hospitalization. Wearable chest sensors can measure impedance, heart rate variability, respiration rate and absolute lung fluid content, helping to reduce heart failure-related hospitalizations by over 80% (Amir et al, 2017). Non-invasive monitoring of lung impedance as a predictor of pulmonary congestion reduces heart failure hospitalizations, heart failure and all-cause mortality (Shochat et al, 2016).

Over the last two decades, the use of specialist nurse-delivered heart failure services in the UK has expanded through integration of hospital-based, outpatient, community and home-based heart failure services (British Heart Foundation, 2008, 2015). This improved quality of life, reduced hospitalizations and lead to considerable cost savings. While there has been some experience in ambulatory management delivered by heart failure specialist nurses (Brightpurpose, 2014; Nyjo et al, 2017; Rawat et al, 2017), larger studies are needed to validate the safety and efficacy of this approach. This will help ambulatory management of patients with acute decompensated heart failure delivered by heart failure specialist nurses to become the new standard of care in the UK. However, it remains to be seen whether existing staffing and financial resources allow the extension of this model throughout the country.

Conclusions

Recurrent hospitalizations as a result of heart failure adversely affect patients' quality of life, morbidity and mortality, and use scarce health-care resources. Evidence from several small studies indicates that ambulatory intravenous diuretic treatment for acute decompensated heart failure in dedicated heart failure units using a multidisciplinary approach,

combined with a robust transitional care programme, can prove a safe, efficacious and cost-effective alternative to hospital admission in eligible patients. Larger studies are needed to support these findings, to enable widespread implementation as standard of care and thereby herald a new era of heart failure management. **BJHM**

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KEY POINTS

- Heart failure is a chronic condition which has significant morbidity and mortality.
- Acutely decompensated heart failure contributes to a considerable proportion of hospitalizations.
- Ambulatory management of acute decompensated heart failure including treatment with intravenous diuretics can potentially be an efficacious and safe alternative to avoid hospitalizations in suitable patients.

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Table 1. Patient demographics

Characteristics	Ryder et al (2008)	Hebert et al (2011)	Lazkani and Ota (2012)	Schipper et al (2012)	Makadia et al (2015)	Buckley et al (2016a)	Banerjee et al (2012)
No of patients	107	130	7	23	106	60	17
Type of study	Retrospective observational	Prospective non-randomized observational cohort	Case series	Non-randomized	Cohort	Retrospective non-randomized cohort	Retrospective non-randomized cohort
Inclusion criteria	Fluid overload secondary to heart failure, not responding to oral diuretic	Inpatients, emergency department, clinic patients aged ≥ 18 years with left ventricular EF $\leq 40\%$	Fluid overload secondary to heart failure, not responding to oral diuretic	Not provided	Treatment of congestion in 'mild' decompensated heart failure	Chronic heart failure, at least one sign and one symptom of decompensation (symptoms included dyspnoea, orthopnoea or oedema, and signs included rales, peripheral oedema or ascites) and, in the opinion of the referring clinician, a high likelihood of needing hospitalization in the near term	Patients with fluid overload secondary to heart failure and reduced EF or normal EF
Unique exclusion criteria	ND	Left ventricular EF $>40\%$	Heart failure patients with acute renal failure	-	Creatinine >2.5 mg/dl, sodium <128 mEq/litre	'Significant comorbidities', massive volume overload (e.g. >10 – 15 lb of estimated fluid weight) or oedema	Pure right heart failure Advanced or end stage chronic kidney disease Patients who require >3 days of treatment
Age (years)	71 (SD=11)	58.2 (SD=13)	55 (range 24–84)	70	68.2–14.2	70 (range 58–80)	70 \pm 6 (range 48–93)
Female	27 (25%)	36 (27%)	3 (43%)	-	50 (47%)	26 (43%)	5 (29.4%)
Ethnicity	-	58 (45%)	-	-	ND	9 (15%)	ND
	-	64 (50%)	-	-	ND	6 (10%)	ND
	-	6 (5%)	-	-	62%	45 (75%)	ND
Heart failure with reduced EF (%)	77 (72%)	130 (100%)	4 (57%)	ND	68 (64)	36 (60%)	16 (94%)
Heart failure with preserved EF (%)	30 (28%)	0	3 (43%)	ND	38 (36)	24 (40%)	1 (6%)
EF (%)	38.4 \pm 14.8 (mean)	23.4 (mean)	-	EF $<40\%$ n = 12 (52%), EF $>40\%$ n = 11 (48%)	39 \pm 18	25% (median EF) for heart failure with reduced EF, 55% (median EF) for heart failure with preserved EF	ND
NYHA class							
1	0	15 (12%)	0	-	8	0	ND
2	9 (8%)	32 (26%)	0	-	139	7 (12%)	ND
3	89 (83%)	35 (29%)	7 (100%)	-	133	35 (58%)	ND
4	9 (8%)	39 (32%)	0	-	ND	12 (20%)	ND
Unknown	-	-	-	-	ND	6 (10%)	ND

Comorbidities	Atrial fibrillation	-	-	-	-	51 (48%)	29 (48%)	9 (53%)	
	Chronic kidney disease	-	-	-	-	61 (58%)	28 (47%)	5 (29%)	
	Diabetes	36 (33%)	59 (45%)	-	-	66 (62%)	31 (52%)	7 (41%)	
	Hypertension	19 (18%)	106 (82%)	-	-	96 (91%)	46 (77%)	9 (53%)	
	Pulmonary hypertension	-	-	-	-	-	6 (10%)	-	
	Chronic obstructive pulmonary disease	26 (24%)	-	-	-	41 (39%)	12 (20%)	5 (29%)	
	Coronary artery disease	75 (70%)	167 (37%)	-	-	68 (64%)	31 (52%)	10 (59%)	
Therapies	Thiazide	-	-	-	-	ND	13 (22%)	-	
	Angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker	84 (78%)	101 (78%)	-	-	76 (72%)	27 (45%)	-	
	Aldosterone antagonist	21 (19%)	27 (21%)	-	-	ND	22 (37%)	-	
	Aspirin	41 (38%)	-	-	-	71 (67%)	-	-	
	Beta blocker	51 (48%)	112 (86%)	-	-	86 (81%)	48 (80%)	-	
	Digoxin	-	38 (29%)	-	-	11 (10%)	11 (18%)	-	
	Nitrates	68 (64%)	-	-	-	13 (12%)	8 (13%)	-	
	Hydralazine	-	-	-	-	12 (11%)	3 (5%)	-	
	Statin	38 (36%)	-	-	-	67 (63%)	-	-	
	Defibrillator	-	-	-	-	ND	31 (52%)	-	
	Cardiac resynchronization therapy	-	-	-	-	ND	16 (27%)	-	
Lab results	Na (mmol/litre)	136.9 (SD=4.1)	137.6	-	-	140 (138-143)	138 (135-140)	-	
	K (mmol/litre)	4.2 (SD=0.7)	-	-	-	4.0 (3.7-4.4)	-	-	
	Urea	13.7 μ mol/litre (SD=7)	4.4	-	-	-	33 mg/dl (23-44)	-	
	Creatinine (μ mol/litre)	153.2 μ mol/litre (SD=72.8)	-	-	-	1.3 mg/dl (1.0-1.8)	1.44 mg/dl (1.43-3.95)	-	
	Estimated glomerular filtration rate (ml/min/1.73m ²)	-	70.5	-	-	-	-	-	
	B-type natriuretic peptide (pg/ml)	1063 (SD=1203)	-	-	-	-	-	-	
	N-terminal pro B-type natriuretic peptide (pg/litre)	-	-	-	-	Median 3204 (range 511-6744)	3533 (1617-6297)	-	
	Systolic blood pressure (mmHg)	126 (SD=25)	135 (SD=28.9)	-	-	-	124 (112-140)	-	
	Diastolic blood pressure (mmHg)	75 (SD=18)	84.9 (SD=17.7)	-	-	-	68 (60-77)	-	
EF = ejection fraction; ND = not defined; NYHA = New York Heart Association; SD = standard deviation									